Effectiveness of Intra-Coronary Injection of Sodium Nitroprusside for the Treatment of Coronary No-Reflow through Punctured Coronary Balloon

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Rapid restoration of thrombolysis in myocardial infarction III in case of no-reflow during percutaneous coronary intervention is imperative. Application of punctured coronary balloon intracoronary injection of sodium nitroprusside is a prompt, safe and effective method. To investigate the effectiveness of intracoronary injection of sodium nitroprusside *via* punctured coronary balloon in the treatment of no-reflow in coronary artery is the main objective of the study. We retrospectively analyzed 76 patients treated with intracoronary injection of sodium nitroprusside *via* punctured coronary balloon for coronary no-reflow. All 76 patients successfully completed intracoronary injection of sodium nitroprusside with the improvement of no-reflow in coronary artery for thrombolysis in myocardial infarction grade III in 74 patients. There were two complications which occurred in the early application of this technique. One was a punctured coronary balloon fracture left in the distal coronary artery and the other was a difficult pullback of the punctured coronary balloon catheter. After improving the application method, later no more complications occurred in 67 patients and no complications such as coronary guide wire pulling out of the coronary artery, coronary artery dissection, coronary artery perforation and coronary artery air embolism occurred. Coronary no-reflow treatment with intracoronary injection of sodium nitroprusside *via* punctured coronary balloon is safe and effective when properly applied.

Key words: Coronary heart disease, percutaneous coronary intervention, sodium nitroprusside, coronary no-reflow

Percutaneous Coronary Intervention (PCI) is the main therapeutic approach for the treatment of Coronary Artery Disease (CAD-Atherosclerosis), which improves patient's symptoms and enhances the survival rate of acute myocardial infarction. However, no-reflow caused by microvascular obstruction during PCI often results in poor patient prognosis[1]. No-reflow is characterized by inadequate perfusion at the myocardial cell level despite the opening of the epicardial coronary arteries and occurs by coronary microcirculatory injury due to distal coronary embolism and ischemia. No-reflow occurs in 0.6 % to 3.2 % of patients undergoing PCI[2], while the incidence of no-reflow in primary PCI can be as high as 5 %-50 %[3]. Use of sodium nitroprusside selectively injected distal to the target coronary artery, can strongly dilate the no-reflow coronary artery and reverse the no-reflow phenomenon with definite efficacy. This study investigated the feasibility of intracoronary injection of sodium nitroprusside *via* the punctured coronary balloon for the treatment of coronary no-reflow. Study population included in this study was explained here. We retrospectively enrolled 76 patients who underwent PCI in our hospital from January 2020 to June 2022, with the intraoperative occurrence of no-reflow and the application of punctured coronary balloon intracoronary injection of sodium nitroprusside for the treatment, of which 41 were males and 35 were females, aged 36-85 y with an average of 69.04±10.61 y old. Inclusion criteria include age≥18 y old; coronary angiography indicated severe coronary artery stenosis-lumen diameter stenosis>75 %; patients who underwent PCI, including drug-eluting stenting, bioresorbable stent, coronary drug balloon dilatation; no-reflow during PCI, defined as coronary flow Thrombolysis In Myocardial Infarction (TIMI) grade 0-2 after coronary balloon dilation or coronary stenting[4]. Exclusion criteria include those with impaired antegrade coronary artery flow due

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to *in situ* thrombosis, dissection, severe spasm and distal embolism. This approach had hospital ethics committee approval and patient's informed consent. Operation method used this study was explained here. All patients underwent coronary angiography and coronary intervention *via* the radial artery with a preoperatively prescribed Aspirin (300 mg), Tegretol (180 mg) or Clopidogrel (600 mg), followed by Aspirin (100 mg once a day (qd)), Tegretol (90 mg two times a day (bid)) or Clopidogrel (75 mg qd). The patient was placed in the supine position and electrocardiographic monitoring and continuous oxygen saturation monitoring were performed; after a successful arterial puncture, dynamic invasive pressure monitoring was performed *via* a four way tee and intraoperative heparin 100 Units/kg was injected. For severe coronary stenosis with lumen diameter stenosis greater than 75 %, PCI including drug-eluting stent implantation, bioresorbable vascular scaffold implantation and percutaneous drug coronary balloon coronary angioplasty was performed. Intraoperative thrombus aspiration was routinely performed for those with white lump in the lumen on coronary angiography indicating a heavy thrombus burden. After coronary balloon dilatation or stenting, TIMI grade 0-2 in the target coronary artery is quickly identified as no-reflow or other causes such as *in situ* thrombosis, dissection, severe spasm or distal embolism. When considered for coronary no-reflow, a Sprinter legend 2.0×15 mm coronary balloon (Medtronic, United States of America (USA)) is injected immediately, to be in dilated shape with sodium nitroprusside at high pressure with a 2 ml syringe. Then the balloon punctured with a black needle fitted to a 5 ml syringe, size 0.72×32 Thin-Walled Long Bevel (TWLB). The punctured coronary balloon is delivered to the distal segment of the targeted coronary artery through the coronary guiding wire, avoiding negative pressure before it was inserted into the guiding catheter to prevent air from returning to the coronary balloon. After the coronary balloon is in place, 200 μg (2 ml) of sodium nitroprusside is administered and the injection is completed within 30-60 s. The 2 ml syringe is withdrawn so that the coronary balloon is deflated and coronary blood is returned. After 1 min, the target artery is observed under fluoroscopy with light contrast agents. If the flow was still less than TIMI grade 3, injection of sodium nitroprusside 200 μg (2 ml) was repeated through the punctured coronary balloon until the coronary blood flow was restored to TIMI grade 3, then the next step of the operation proceeded. Statistical analysis explained in this study was as follows. Whether the distribution of continuous variables was normal or not, it was evaluated *via* the Kolmogorov-Smirnov test. Continuous data with a normal distribution were expressed as mean±standard deviation. The count data were expressed as percentages. The study population's demographic, clinical, laboratory and procedural characteristics are listed in Table 1. All 76 patients with no-reflow coronary artery were treated with an intracoronary injection of sodium nitroprusside into the punctured coronary balloon and restored TIMI grade 3 flow. There were two patients that presented stubborn no reflow, TIMI grade 0, one was after stent implantation when the right coronary Chronic Total Occlusion (CTO) was opened and the other was after the stent implantation for the long lesions in the middle segment of the circumflex branch. After repeated application of six times of sodium nitroprusside 200 μg by punctured coronary balloon delivered to the distal segment of the targeted coronary artery, the operation ended without reflow improvement. Later, in two patients both showed refractory heart failure, which significantly prolonged the hospital stay. There were two related complications: One case was the disconnection of the distal segment of the punctured coronary balloon, which later flowed into the small side coronary branch and caused side branch infarction; the other case was the difficult pullback of the punctured coronary balloon catheter, which was embedded in the distal trabeculae of the coronary stent. The catheter was pulled out vigorously, later stent disfigurement caused. There were no complications in the next 68 patients and no complications such as coronary guiding wire pulling out of the coronary artery, coronary artery dissection, coronary artery perforation and coronary artery air embolism occurred in 76 patients. Coronary artery no-reflow is a particular complication that should be watched out in PCI treatment[4]. No-reflow inhibits flow exchange in the myocardial ischemic zone, prevents healing of the myocardial necrotic zone, delays ventricular remodeling, increases the incidence of heart failure[5] and is an independent predictor of rehospitalization, malignant arrhythmias and heart failure, recurrent myocardial infarction, and cardiovascular death in patients after PCI[6].

TABLE 1: THE STUDY POPULATION CHARACTERISTICS

Variable	Numerical value
Gender (F/M)	35/41
Smoking history (%)	34
Drinking alcohol (%)	21
Hypertension (cases)	36
Diabetes mellitus (cases)	30
Age (years)	63.87±10.31
Body mass index (Kg/m^2)	22.10±2.52
Blood glucose (mmol/l)	6.08±2.18
Total cholesterol (mmol/l)	4.16±0.77
Triglycerides (mmol/l)	1.85±1.11
Low-density lipoprotein (LDL, mmol/l)	2.51±0.69
High-density lipoprotein (HDL, mmol/l)	1.08±0.23
High-Sensitivity C-Reactive Protein (HCRP, mmol/l)	5.67±2.30
Blood Urea Nitrogen (BUN, mmol/l)	7.29±7.03
Creatinine (CR, μmol/l)	94.22±21.8
Maximum coronary balloon dilation pressure (Atm)	17.70±2.68
Number of stents implanted (pcs)	1.30±0.46
TIMI grade 0 at the time of no-reflow occurrence (cases)	27
TIMI grade 1 at the time of no-reflow (cases)	34
TIMI grade 2 at the time of no-reflow (cases)	15
Administration of sodium nitroprusside 200 μg times	1.34±0.72
Preoperative Troponin I (TnI, ng/l)	6.13±6.68
TnI (ng/l) at 24 h postoperatively	6.80±6.87

Although the mechanism of coronary artery no-reflow is currently poorly understood, studies have demonstrated that the occurrence of no-reflow is associated with microvascular disorders, including distal micro-thromboembolism, reperfusion injury and endothelial dysfunction[7]. Several cardiovascular risk factors, such as over 65 y of age, hypertension, smoking, dyslipidemia, diabetes mellitus, renal failure, inflammatory response and history of atrial fibrillation, as well as factors associated with PCI, such as heavy thrombus burden, delayed PCI, and coronary balloon hyperbaric dilation within coronary lesions are high-risk factors for the development of no-reflow[8]. Sodium nitroprusside is a commonly used drug for coronary artery dilation, with its active metabolite nitric oxide, it potently dilates the coronary microcirculation and inhibits platelet aggregation with a longer duration of action than calcium antagonists, a lower incidence of adverse events, faster flow velocity recovery and ST-segment regression, and a more preserved left ventricular ejection fraction compared to agents such as tirofiban[9,10]. When coronary artery no-reflow occurs, patients present symptoms of chest pain and irritability, often with haemodynamics instability and malignant arrhythmias. Rapid restoration of blood flow TIMI grade 3 is required at this time is imperative. Sodium nitroprusside 200 μg injected to the distal target artery is effective in improving no-reflow, restoring coronary flow TIMI class 3, improves symptoms and prognosis[11]. There are three conventional approaches for distal segment administration of no-reflow, which use microcatheter, rapid exchange balloon dilatation catheter, or aspiration catheter. The use of microcatheter requires an anchor of coronary guide wire for pushing microcatheter into the distal coronary artery and then drawing out the coronary guide wire after microcatheter is in place, which increases the operation process and time, while punctured coronary balloon being in place takes approximately only 35 s. Rapid exchange balloon dilatation catheter is more expensive and is not widely used in clinical practice, many catheterization laboratories are not equipped; aspiration catheter, which has a thicker diameter, affects the monitoring of invasive arterial blood pressure in the guiding

catheter after drug administration. To avoid the above shortcomings, we have used a punctured coronary balloon to administer sodium nitroprusside in the distal segment of the coronary target artery in the past years, successfully treated 76 patients without no-reflow, restored coronary blood flow TIMI grade 3 quickly and effectively. However, two complications occurred during the early use of this method. In the first complication, which occurred in the 6th patient who received this approach, the distal segment of the punctured coronary balloon was disconnected during withdrawing and the disconnected end of the coronary balloon rushed into the small side branch causing the side branch infarcted. The reason for this was that the operator used a needle (size 1.2×30 TWLB) equipped in a 50 ml syringe to puncture the coronary balloon. The tip of the needle was too large and damaged the central rod of the coronary balloon, which became disconnected during the pull back. In the second complication, which occurred in the 9th patient with this method, the punctured coronary balloon had difficulty in pull back after drug administration, in that the operator chose the coronary balloon puncture point located at the coronary balloon body instead of the tip of the coronary balloon head. The coronary balloon was embedded in the distal trabeculae of the coronary stent, making forward delivery and retraction difficult. Subsequently, the coronary balloon was forcefully pulled out, which caused the original coronary stent retracted and disfigured. A rescuing non-compliant balloon of 20 Atmosphere (Atm) was performed, after that a drug-eluting stent was implanted for remodeling. After improving the application method by summarizing the experience, no further complications occurred during the subsequent application in 67 patients. Our experience was as follows. Considering the passability of the punctured coronary balloon, a compliant coronary balloon with good passability should be chosen. Sprinter legend 2.0×15 mm coronary balloon is appropriate. The diameter of the coronary balloon is too small to be convenient to tie the hole and the coronary balloon is too large and long to have smooth passability. The needle for the puncture should be chosen from the black needle (specification 0.72×32 TWLB) that comes with the 5 ml syringe and one needle eye can be tied. A smaller needle shows no benefit for drug injection; a larger needle tends to damage the coronary balloon rod which caused disconnection and a broken section that may cut the stent trabeculae and embed will appear. The coronary balloon puncture point should be selected at the tip of the coronary balloon head, so that the whole balloon can be deflated when pumped back under negative pressure, thus avoiding embedding when the coronary balloon is drawn back. Apply 2 ml syringe of pre-sufficient sodium nitroprusside to connect the coronary balloon and then pressurize to fill the balloon, then avoid negative pressure air bolus into the coronary balloon until the coronary balloon enters the guideline catheter, so that the coronary balloon can administer drug once in place without pumping back to see the blood, which greatly saves time. When dragging out the punctured coronary balloon catheter, the entire coronary segment must be fluoroscoped, dragging without resistance. In the case of resistance of retraction in the coronary stent, the retraction should be stopped and the coronary balloon should be sent forward to rotate at a certain angle and then retracted again carefully, so as to avoid the coronary balloon rupture or embedded in the stent trabeculae. For people with a high risk of no-reflow, a punctured coronary balloon standby will turn no-reflow first aid more quickly. The goal of PCI was to achieve coronary flow TIMI grade 3 and restoration of coronary flow TIMI grade 3, improved left ventricular function, and reduced congestive heart failure and mortality. The Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) trial found that patients with TIMI grade 3 had a significantly higher survival rate than patients with TIMI grade 0, 1 or 2 at 2 y[12]. Intracoronary injection of sodium nitroprusside *via* punctured coronary balloon for coronary artery no-reflow restores coronary flow TIMI grade 3 rapidly and safely without exchange of coronary guidewire and without interfering with invasive arterial blood pressure monitoring. For coronary compliance, coronary balloons are less expensive and more accessible than microcatheter, rapid exchange balloon dilatation catheter and aspiration catheter. The correct application of punctured coronary balloon intracoronary injection of sodium nitroprusside for coronary artery with no-reflow is safe and effective. The number of subjects in this study is relatively small and further experience with its use is needed.

Conflict of interests:

The authors declared no conflict of interest.

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This article was originally published in a special issue, "Current Trends in Pharmaceutical and Biomedical Sciences" Indian J Pharm Sci 2022:84(5) Spl Issue "10-14"