Effectiveness of Intra-coronary Injection of Sodium Nitroprusside to The Treatment of Coronary No-Reflow Through Punctured Coronary Balloon

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Abstract

Background

Rapid restoration of TIMI 3 on case of no-reflow during PCI is imperative. Application of punctured coronary balloon intracoronary injection of sodium nitroprusside is a prompt, safe and effective method.

Objective

To investigate the effectiveness of intracoronary injection of Sodium Nitroprusside via punctured coronary balloon in the treatment of no-reflow in coronary artery. Methods: We retrospectively analyzed 76 patients treated with intracoronary injection of Sodium Nitroprusside via punctured coronary balloon for coronary no-reflow.

Results

All 76 patients successfully completed intracoronary injection of Sodium Nitroprusside, with the improvement of no-reflow in coronary artery to TIMI grade III in 74 patients. There were two complications 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 pullbacking of the punctured coronary balloon catheter. After improving the application method, no more complication case occurred in 67 cases afterward, and no complications such as coronary guide wire pulled out of the coronary artery, coronary artery dissection, coronary artery perforation, and coronary artery air embolism occurred.

Conclusion

Coronary no-reflow treatment with intracoronary injection of Sodium Nitroprusside via punctured coronary balloon is safe and effective when properly applied.

Introduction

Percutaneous Coronary Intervention (PCI) is the main therapeutic approach for the treatment of coronary atherosclerotic heart disease (CAD), which improves patients’ 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 0.6–3.2% 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.

**Methods**

**Study population**

We retrospectively enrolled 76 patients who underwent percutaneous coronary intervention 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 whom 41 were males and 35 were female, 36–85 (69.04 ± 10.61) age years old. Inclusion criteria: (1) Age ≥ 18 years old. (2) Coronary angiography indicated severe coronary artery stenosis: lumen diameter stenosis > 75%. (3) Underwent PCI, including drug-eluting stenting, bioresorbable stenting, coronary drug balloon dilatation. (4) No-reflow during PCI, defined as coronary flow TIMI grade 0–2 after coronary balloon dilation or coronary stenting [4]. Exclusion criteria: those with impaired antegrade coronary artery flow due to in situ thrombosis, dissection, severe spasm, and distal embolism. This approach had hospital ethics committee approval and patient’s informed consent.

Operation method: All patients underwent coronary angiography and coronary intervention via the radial artery with a preoperative prescribed Aspirin (300mg), Tegretol (180mg), or Clopidogrel (600mg), followed by Aspirin (100mg qd), Tegretol (90mg bid) or Clopidogrel (75mg 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 u/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 load. 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*15mm coronary balloon (Medtronic, USA) is injected immediately to be dilated shape with sodium nitroprusside at high pressure with a 2ml syringe, then the balloon punctured with a black needle fitted to a 5ml 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 inserted into the guiding catheter to prevent air from returning to the coronary balloon. After the coronary balloon is in place, 200ug (2ml) of sodium nitroprusside is administered, and the injection is completed within 30-60S. The 2ml syringe is withdrawn so that the coronary balloon is deflated and coronary blood is returned. After 1 minute, the target artery is observed under fluoroscopy with light contrast. If the flow was still less than TIMI grade 3, injection of
sodium nitroprusside 200ug (2ml) 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**

Whether the distribution of continuous variables was normal 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.

**Results**

The study population's demographic, clinical, laboratory, and procedural characteristics are listed in Table 1.
### Table 1
The study population's characteristic

<table>
<thead>
<tr>
<th>Variable</th>
<th>Numerical value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>35/41</td>
</tr>
<tr>
<td>Smoking history(%)</td>
<td>34</td>
</tr>
<tr>
<td>Drinking alcohol (%)</td>
<td>21</td>
</tr>
<tr>
<td>Hypertension (cases)</td>
<td>36</td>
</tr>
<tr>
<td>Diabetes mellitus (cases)</td>
<td>30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.87 ± 10.31</td>
</tr>
<tr>
<td>Body mass index (Kg/M2)</td>
<td>22.10 ± 2.52</td>
</tr>
<tr>
<td>Blood Glucose(mmol/l)</td>
<td>6.08 ± 2.18</td>
</tr>
<tr>
<td>Total cholesterol(mmol/l)</td>
<td>4.16 ± 0.77</td>
</tr>
<tr>
<td>Triglycerides(mmol/l)</td>
<td>1.85 ± 1.11</td>
</tr>
<tr>
<td>Low-density lipoprotein LDL(mmol/l)</td>
<td>2.51 ± 0.69</td>
</tr>
<tr>
<td>High-density lipoprotein HDL(mmol/l)</td>
<td>1.08 ± 0.23</td>
</tr>
<tr>
<td>High-sensitivity C-reactive protein HCRP(mmol/l)</td>
<td>5.67 ± 2.30</td>
</tr>
<tr>
<td>Urea nitrogen BUN(mmol/l)</td>
<td>7.29 ± 7.03</td>
</tr>
<tr>
<td>Creatinine CR(umol/l)</td>
<td>94.22 ± 21.8</td>
</tr>
<tr>
<td>Maximum Coronary balloon Dilation Pressure(ATM)</td>
<td>17.70 ± 2.68</td>
</tr>
<tr>
<td>Number of Stents Implanted(pcs)</td>
<td>1.30 ± 0.46</td>
</tr>
<tr>
<td>TIMI grade 0 at the time of no-reflow occurrence (cases)</td>
<td>27</td>
</tr>
<tr>
<td>TIMI grade 1 at the time of no-reflow (cases)</td>
<td>34</td>
</tr>
<tr>
<td>TIMI grade 2 at the time of no-reflow (cases)</td>
<td>15</td>
</tr>
<tr>
<td>Administration of sodium nitroprusside 200ug times</td>
<td>1.34 ± 0.72</td>
</tr>
<tr>
<td>Preoperative TnI(ng/l)</td>
<td>6.13 ± 6.68</td>
</tr>
<tr>
<td>TnI(ng/l) at 24 hours postoperatively</td>
<td>6.80 ± 6.87</td>
</tr>
</tbody>
</table>

All 76 cases 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 related complications: There were two patients that presented stubborn no reflow, TIMI grade 0, one was after stent implantation when the right coronal 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 200ug times by punctured coronary balloon delivered to the distal segment of the targeted coronary artery, the operation ended without reflow improvement. Later, the 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 pullbacking of the punctured coronary balloon catheter, which was embedded in the distal trabeculae of the coronary stent. The catheter pulled out vigorously later, stent disfigurement caused. There were no complications in the next 68 cases, 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 cases.

Discussion

Coronary artery no-reflow is a particular complication that should be watched out in PCI treatment [5]. 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 [6], and is an independent predictor of rehospitalization, malignant arrhythmias, and heart failure, recurrent myocardial infarction, and cardiovascular death in patients after PCI [7]. 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 [8]. Several cardiovascular risk factors, such as over 65 years of age, hypertension, smoking, dyslipidemia, diabetes mellitus, renal failure, inflammatory response, and history of atrial fibrillation, as well as factors associated with surgery, such as heavy thrombus load, delayed PCI, and coronary balloon hyperbaric dilation within coronary lesions are high-risk factors for the development of no-reflow [9].

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 [10] [11].

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 200µg injected to the distal target artery is effective in improving no-reflow, restoring coronary flow TIMI class 3, improving symptoms and prognosis [12]. There are three conventional approaches for distal segment administration of no-reflow, which are use microcatheter, rapid exchange balloon dilatation catheter, or Aspiration catheter. Microcatheter’s use must first anchor coronary guide wire for pushing microcatheter into the distal coronary and then draw out the
coronary guide wire after microcatheter is in place, which increases the operation process and time, while Punctured coronary balloon being in place is approximately only 35 seconds. Rapid exchange balloon dilatation catheter is more expensive and is not widely used in clinical practice, many catheterization laboratories 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 case, who is the sixth patient received the 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*30TWLB) 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 pulling back. In the second complication, which occurred in the ninth patient with this method, the punctured coronary balloon had difficulty in pulling 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 resucing non-compliant balloon of 20 ATM was performed, after that a drug-eluting stent 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: 1. Considering the passability of the punctured coronary balloon, a compliant coronary balloon with good passability should be chosen. Sprinter legend 2.0*15mm 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. 2. The needle for the puncture should be chosen from the black needle (specification 0.72*32TWLB) that comes with the 5ml syringe, and one needle eye can be tied. A smaller needle is not benefit for drug injection; A larger needle tend to damage the coronary balloon rod caused disconnection, and a broken section that may cut the stent trabeculae and embed will appear. 3. 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. 4. Apply 2ml syringe 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. 5. When dragging out the punctured coronary balloon catheter, the entire coronary segment must be fluoroscopyed, 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. 6. 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 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 two years [13]. 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. 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 cases in this study is relatively small, and further experience with its use is needed.

Declarations

The Corresponding Author, also on behalf of the other Authors, represents and warrants:

1. Ethics approval and consent to participate: The study has been conducted in accordance with the principles set forth in the Helsinki Declaration. The study was approved by the Institutional Ethical Committee of Yongkang First People's Hospital (protocol number: ykyy 2020-05). Patients have given their informed consent for participation in the research study.

2. Consent for publication: The Authors have obtained permission from the patients of the study to publish their identifiable data in an online, open-access journal.

3. Availability of data and materials: The datasets used during the current study available from the corresponding author on reasonable request.

4. Competing interests: The authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and discussion reported in this paper.

5. Funding: No.

6. Authors' contributions: Yunxiang Wang carried out the studies, wrote the main manuscript text and Changchun Lai prepared figures 1.

7. Acknowledgements: No.

References


