Radionuclide angiography after nisoldipine to detect myocardial viability

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Abstract

Introduction: Myocardial viability determines prognosis in patients with prior myocardial infarction and poor ventricular function submitted to percutaneous transluminal coronary angioplasty (PTCA).

Objectives: To detect viability in the infarcted zone with the use of nisoldipine, a calcium channel blocker with selective coronary vasodilation properties.

Material and Methods: Twenty infarcted patients (mean age: 47± 8 years; 15 men and 5 women) were studied.

Three radionuclide angiographies in 35-degree left anterior oblique, anterior and 70-degree lateral projections were performed: at rest, one hour after 10 mg oral nisoldipine, and 2 months after PTCA.

Results: Of 89 segments with reduced contractility at rest, 37 improved following nisoldipine and PTCA, while 11 only did it after PTCA. Left ventricular ejection fraction (LVEF) increased from 45± 11% to 51± 10% postnisoldipine (p<0.001) and to 51± 11% post PTCA (p<0.001). Peak filling rate and stroke volume increased without statistical significance. End-systolic volume decreased significantly from 134± 35 ml to 114± 41 ml postnisoldipine, and to 125± 51 ml post PTCA (p<0.001).

Discussion: Nisoldipine produces arterial vasodilation with the consequent afterload and end-diastolic left ventricular pressure reduction. This originates a transient flow increase to the ischemic zone, with a demonstrable effect on left ventricular wall motion and also on perfusion of viable zones. The comparable hemodynamic response and wall motion improvement in postnisoldipine and post PTCA tests observed in this study, permits the prediction of post PTCA functional recovery by nisoldipine testing. Nevertheless, in spite of the nisoldipine's alleged "selective" coronary effect, there is also a systemic effect with afterload decrease which can explain the significant reduction of blood pressure observed in our patients. This could also originate the LVEF improvement after nisoldipine administration. To exclude this possibility, we considered that there was viability only when LVEF increased 3 4 units following wall motion improvement in previously affected segments.

Conclusions: Postnisoldipine radionuclide angiography is a useful method to detect myocardial viability and predict post PTCA functional recovery.

Introduction

The primary function of the heart is to pump and one of the most serious manifestations of myocardial ischemia is contractile dysfunction. When regional contractile dysfunction is the result of either chronic or repetitive episodes of acute ischemia, restoration of perfusion due to interventions such as thrombolysis, percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting, will eventually improve regional function. Jeopardized myocardium that improves function after appropriate reperfusion is considered viable in contrast with persistently dysfunctional, non viable myocardium, caused by infarction. Thus, definite evidence of myocardial viability is the temporal improvement in contractile function irrespective of the etiology of dysfunction or the specific intervention used.

Among imaging techniques, conventional radionuclide imaging is widely used to assess myocardial viability and, in general, thallium-201 (201TI) imaging has a high sensitivity, but a relatively low specificity.
for predicting left ventricular functional recovery.

With radionuclide angiography, when the coronary blood flow increases due to an adequate pharmacological intervention, an increase in left ventricular ejection fraction (LVEF), as well as an improvement of regional contractility in a previously affected segment, is generally observed.

This intervention can be simulated with a short-acting nitrate as nitroglycerin or with isosorbide dinitrate. For the same purpose we have also used calcium channel blockers of the dihydropyridines group, due to their vasodilatory effect.

**Objectives**

To detect viability in the infarcted zone with the use of nisoldipine, a calcium channel blocker with selective coronary vasodilation properties.

**Materials and Methods**

**Patients**

Twenty consecutive patients who had a previous Q-wave myocardial infarction (MI), who were referred to our nuclear medicine laboratory for functional evaluation of coronary artery disease previous a PTCA procedure, were included. All patients had symptoms with episodes of stable angina class II (n=14) and class III (n=6). The mean basal LVEF was 45%. Characteristics of patients are summarized in Table 1.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>PATIENT CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients:</td>
<td>20</td>
</tr>
<tr>
<td>Sex (M / F):</td>
<td>15 / 5</td>
</tr>
<tr>
<td>Age (years): Mean: 47 Minimum: 32 Maximum: 61</td>
<td></td>
</tr>
<tr>
<td>MI localization: Anterior 15 Inferior 5 Anterior / Inferior 0 Lateral 0</td>
<td></td>
</tr>
<tr>
<td>MI evolution time (months) (mean ± SD): 5 ± 6</td>
<td></td>
</tr>
<tr>
<td>Coronary angiography:</td>
<td></td>
</tr>
<tr>
<td>Three-vessel CAD: 4 Two-vessel CAD: 7 One-vessel CAD: 9</td>
<td></td>
</tr>
</tbody>
</table>

*MI = myocardial infarction; CAD = coronary artery disease*

**Study protocol**

All patients were studied after withdrawal of calcium channel blocker therapy for at least 72 hours; all other medication was continued.

Every patient underwent three radionuclide angiography: the first under baseline conditions; the second one hour after 10 mg oral nisoldipine administration and the last one, 2.5 ± 1 months after the PTCA procedure.

**Radionuclide angiography**

After in vivo labeling of red blood cells with 17 MBq of technetium-99m (99mTc) per kg of body weight, imaging was performed with a digital gamma camera (GCA 501S, Toshiba) in the 35-degree left anterior oblique, anterior and 70-degree lateral projections. Sixteen 64x64 frames corresponding to an average cardiac cycle were acquired until 3 x106 counts were accumulated. Cycles with periods outside ± 10% of the average were rejected. Images were filtered for space-time high-frequency noise. A left ventricular region of interest was constructed in end-diastolic and in end-systolic images. Background was determined from a periventricular region of interest in the end-diastolic image. The LVEF was determined by the standard method.
A significant change in postnisoldipine or post PTCA radionuclide angiography was defined by modification of the global LVEF of 3-4 units compared with the baseline value, as well as an improvement of wall motion in the previously affected segments. The choice of the threshold of 4 ejection fraction units was based on the radionuclide angiography reproducibility in our laboratory.

For regional wall motion analysis, each projection was divided as follows:

- Anterior: anterolateral, inferior, and apical segments.
- 35-degree left anterior oblique: septal, inferoapical, and posterolateral segments.
- 70-degree lateral: anterior, posterior, and apical segments.

The motion of each segment was evaluated with the following score: 0 = normokinesis, 1 = mild hypokinesis, 2 = severe hypokinesis, 3 = akinesis, and 4 = dyskinesis. According to the comparison between the basal, postnisoldipine and post PTCA scores, each asynergic segment was classified as either improved (wall motion score decrease 3-1 grade) or unchanged.

Peak filling rate was determined as the maximum positive of dV/dt. It was divided by the maximum number of counts and was expressed as the number of times the end-diastolic volume (EDV) per second (EDV/sec).

The EDV was calculated by the Simpson method. We calculated this parameter in a control group of 81 healthy volunteers, obtaining a normal value of 124±12 ml for men and 100±13 ml for women (mean ± 2 SD). We also calculated the end-systolic volume (ESV) and the stroke volume (SV) using the following formulae:

\[
ESV = (1 - LVEF) \times EDV
\]

\[
SV = EDV - ESV
\]

In our control group of 81 healthy volunteers, the obtained normal values were (for men and women, respectively): ESV: 40±8 ml and 32±7 ml; SV: 85±16 ml and 68±11 ml. These values are expressed as mean ± 2 SD.

Statistical analysis

Values were reported as the mean ± standard deviation. Continuous variables were analyzed using Wilcoxon's signed rank test (for heart rate and arterial blood pressure); otherwise Friedman's test was used and, when the obtained value was significant, the intergroup difference was analyzed with the Wilcoxon's signed rank test. Discrete variables were analyzed using McNemar's test. A probability value of p < 0.05 was considered significant.

Results

Complete revascularization of all stenosed major coronary epicardial vessels were achieved using multiple PTCA (either with balloon or stent) in all patients.

Table 2 shows the hemodynamic behaviour postnisoldipine and post PTCA. Although there was no significant change in heart rate, both systolic and diastolic blood pressure decreased after nisoldipine administration.
The LVEF increased from 45 ± 11% to 51 ± 10% post nisoldipine and to 51 ± 11% post PTCA.

Peak filling rate and stroke volume showed a tendency to increase, however this was not significant. End-systolic volume decreased significantly from 134 ± 35 ml to 114 ± 41 ml post nisoldipine, and to 125 ± 51 ml post PTCA.

A total of 180 segments were analyzed. Under baseline conditions, 91 (51%) had normal wall motion, while 89 (49%) were asynergic: 80 hypokinetic and 9 akinetic.

Of the 80 hypokinetic segments, 35 showed wall motion improvement both post nisoldipine and post PTCA; while 8 only did it post PTCA (figure 1). Of the 9 akinetic segments, 2 had wall motion improvement both post nisoldipine and post PTCA, and 3 only did it post PTCA (figure 2). No significant difference was found between post nisoldipine and post PTCA wall motion behaviour, neither for hypokinetic nor akinetic segments.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>BASELINE</th>
<th>POST NISOLDIPINE</th>
<th>POST ANGIOPLASTY</th>
<th>STATISTICAL SIGNIFICANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>66 ± 11</td>
<td>65 ± 10</td>
<td>65 ± 12</td>
<td>p NS</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>124 ± 21</td>
<td>122 ± 22</td>
<td>—</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>84 ± 11</td>
<td>81 ± 10</td>
<td>—</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>45 ± 11</td>
<td>51 ± 10*</td>
<td>51 ± 11</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Peak filling rate (EDV/sec)</td>
<td>173 ± 52</td>
<td>183 ± 53</td>
<td>180 ± 55</td>
<td>p NS</td>
</tr>
<tr>
<td>End-diastolic volume (cml)</td>
<td>249 ± 65</td>
<td>232 ± 68</td>
<td>258 ± 92</td>
<td>p NS</td>
</tr>
<tr>
<td>End-systolic volume (ml)</td>
<td>134 ± 55</td>
<td>114 ± 41</td>
<td>125 ± 51</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>118 ± 51</td>
<td>118 ± 49</td>
<td>127 ± 67</td>
<td>p NS</td>
</tr>
</tbody>
</table>

EDV: end-diastolic volume. Values are expressed as mean ± standard deviation.
* Statistical significance between baseline and post nisoldipine values.

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No significant difference was found in LVEF between postnisoldipine and post PTCA studies. In 3 patients
LVEF decreased comparing baseline and post PTCA studies.

**Discussion**

It is well known that the recovery of left ventricular function after revascularization is more likely to occur in patients whose left ventricular dysfunction is related to viable, hibernating myocardium rather than to irreversible myocardial damage, and that reversal of ischemia after MI is worthwhile only if viability exists in a sufficiently large portion of the left ventricle.

In previous studies we also used nisoldipine as vasodilator, because dihydropyridines produce arterial vasodilation with the consequent afterload and end-diastolic left ventricular pressure reduction. This originates a transient flow increase to the ischemic zone, with a demonstrable effect on left ventricular wall motion and also on perfusion of viable zones.

We studied previously 20 infarcted patients with LVEF < 50% in whom no significant difference in viability diagnosis was found between postnisoldipine radionuclide angiography and stress / redistribution / reinjection 201Tl scintigraphy. The comparable hemodynamic response and wall motion improvement in postnisoldipine and post PTCA tests observed in the present study, permits the prediction of post PTCA functional recovery by nisoldipine testing.

Nevertheless, it is important to point out that, in spite of the nisoldipine's alleged "selective" coronary effect, there is also a systemic effect with afterload decrease which can explain the significant reduction of blood pressure observed in our patients. This could also originate the LVEF improvement after nisoldipine administration. However, to exclude this possibility, we considered that there was viability only when LVEF increased 3-4 units following wall motion improvement in previously affected segments.

**Conclusions**

Postnisoldipine radionuclide angiography is a useful method to detect myocardial viability and predict post PTCA functional recovery.

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