Acute Hyperglycemia Attenuates Coronary Flow Reserve in Patients with Glucose Intolerance

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Background

- It has been reported that acute hyperglycemia is independently associated with worse prognosis in patients with myocardial infarction.
  
  Ceriello A. Eur Heart J 2005;26:328-331

- Acute hyperglycemia itself causes peripheral vascular endothelial dysfunction in patients with impaired glucose tolerance.
  

- However, the association between acute hyperglycemia and coronary microcirculation is still unclear
Purpose

To investigate the influences of acute hyperglycemia induced by oral glucose tolerance test (OGTT) on coronary flow reserve (CFR)
Subjects
Fifty-two patients without known diabetes mellitus.
Patients were divided into following 3 groups according to OGTT results.

- group N: Normal glucose tolerance
- group IGT: Impaired glucose tolerance
- group DM: Diabetes mellitus

Exclusion criteria:
- old myocardial infarction
- previous cardiac surgery
- idiopathic cardiomyopathy
- left ventricular hypertrophy
- no sinus rhythm
- artificial pacemaker
Methods: CFR during OGTT

Echo Machine: SIEMENS Sequoia 512, 3.5~7.0 MHz transducer

The examination started at 9:00 am after fasting for at least 8 hours.

CFR measurement (CFRpre)  
(30min)

75g glucose administration

CFR measurement (CFRpost)  
(60min)  
(120min)

Blood sampling: glucose and insulin concentration
Methods: Coronary Flow reserve

\[ CFR = \frac{\text{Mean diastolic flow velocity at hyperemia}}{\text{Mean diastolic flow velocity at baseline}} \]

( hyperemia was induced by intravenous infusion of ATP 0.15 mg/kg/min)

Changes in CFR (c-CFR)

\[ \text{Changes in CFR (c-CFR)} = \frac{\text{CFR (post)} - \text{CFR (pre)}}{\text{CFR (pre)}} \times 100 \ (\%) \]
### Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>N (n=23)</th>
<th>IGT (n=16)</th>
<th>DM (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>58±13</td>
<td>58±10</td>
<td>60±11</td>
</tr>
<tr>
<td>Men/Women (%Men)</td>
<td>17/6(74%)</td>
<td>14/2(88%)</td>
<td>11/2(85%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.9±3.6</td>
<td>25.5±2.8*</td>
<td>25.7±2.8*</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>7 (30%)</td>
<td>6 (31%)</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>201±39</td>
<td>205±35</td>
<td>184±33</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>59±21</td>
<td>50±12</td>
<td>45±10*</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>117±36</td>
<td>125±32</td>
<td>113±40</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>127±51</td>
<td>143±78</td>
<td>151±72</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>93±3</td>
<td>94±8</td>
<td>110±7**</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>7.6±4.1</td>
<td>10.4±5.5</td>
<td>12.8±7.4**</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5.1±0.3</td>
<td>5.4±0.3**</td>
<td>5.6±0.1**</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01 vs N group. Data are expressed as mean ±SD.
N = Normal glucose tolerance, IGT = Impaired glucose tolerance, DM = Diabetes mellitus, HDL = High-density lipoprotein, LDL = Low-density lipoprotein, HbA1C = Glycohemoglobin A1C.
Changes in glucose concentration before, 1 hour and 2 hours after glucose loading

*Changes in glucose concentration before, 1 hour and 2 hours after glucose loading.*

Graph showing glucose levels in different groups (N, IGT, DM) before, 1 hour, and 2 hours after glucose loading.

- Before: N and IGT have similar glucose levels, with DM slightly higher.
- 1 hour: DM shows the highest increase, followed by IGT, with N showing a lower increase.
- 2 hours: DM continues to have the highest glucose levels, with IGT and N showing moderate increases.

Statistical significance:
- p<0.0001
- p=NS
- p<0.0001
- p=0.007
- p=0.0001
- p<0.0001
- p<0.0001
- p<0.0001

Legend:
- N: Normal
- IGT: Impaired Glucose Tolerance
- DM: Diabetic
Changes in insulin concentration before, 1 hour and 2 hours after glucose loading

Insulin concentration is shown in μU/ml. The graph illustrates the changes in insulin concentration before and after glucose loading for different groups: N, IGT, and DM. The p-values indicate statistical significance:

- p=0.007
- p=NS
- p=0.008
<table>
<thead>
<tr>
<th></th>
<th>before</th>
<th>1 hour after</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart rate (bpm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N group</td>
<td>59 ± 9</td>
<td>62 ± 10</td>
<td>0.04</td>
</tr>
<tr>
<td>IGT group</td>
<td>57 ± 8</td>
<td>59 ± 10</td>
<td>0.04</td>
</tr>
<tr>
<td>DM group</td>
<td>62 ± 11</td>
<td>63 ± 12</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N group</td>
<td>126 ± 14</td>
<td>127 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>IGT group</td>
<td>137 ± 14</td>
<td>138 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>DM group</td>
<td>134 ± 15</td>
<td>132 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N group</td>
<td>74 ± 9</td>
<td>75 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>IGT group</td>
<td>80 ± 10</td>
<td>82 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>DM group</td>
<td>82 ± 11</td>
<td>79 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Double product</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N group</td>
<td>7464 ± 1483</td>
<td>7822 ± 1416</td>
<td>0.02</td>
</tr>
<tr>
<td>IGT group</td>
<td>7796 ± 1418</td>
<td>8098 ± 1416</td>
<td>NS</td>
</tr>
<tr>
<td>DM group</td>
<td>8433 ± 2183</td>
<td>8731 ± 1911</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Cardiac output (l/min)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N group</td>
<td>5.0 ± 1.2</td>
<td>5.5 ± 1.8</td>
<td>0.0008</td>
</tr>
<tr>
<td>IGT group</td>
<td>5.4 ± 1.0</td>
<td>5.6 ± 1.1</td>
<td>0.01</td>
</tr>
<tr>
<td>DM group</td>
<td>5.6 ± 1.7</td>
<td>5.9 ± 1.9</td>
<td>0.04</td>
</tr>
</tbody>
</table>
N case

Baseline

Hyperemia

before loading
CFR = 4.0

1 h after loading
CFR = 2.9
IGT case

before loading
CFR = 3.3

1 h after loading
CFR = 2.8

Baseline

Hyperemia
DM case

Baseline

Hyperemia

before loading
CFR = 2.6

1 h after loading
CFR = 2.0
Mean diastolic velocity (MDV) before and 1 hour after glucose loading in N group

MDV (cm/sec.)

Baseline (before)  Hyperemia (before)  Baseline (1 h)  Hyperemia (1 h)

23 ± 7  69 ± 19  26 ± 8  67 ± 19

p = 0.006  p = NS
Mean diastolic velocity (MDV) before and 1 hour after glucose loading in IGT group

Baseline (before) Hyperemia (before) Baseline (1 h) Hyperemia (1 h)

24±8 70±22 26±10 64±22

p=NS

p=0.02
Mean diastolic velocity (MDV) before and 1 hour after glucose loading in DM group

Baseline (before) | Hyperemia (before) | Baseline (1 h) | Hyperemia (1 h)

21 ± 7 | 65 ± 27 | 24 ± 4 | 53 ± 20

p=NS

p=0.003
CFR changes before and 1 hour after glucose loading

CFR (N)

before | 1 hour
---|---
3.0±0.5 | 2.6±0.5

**p=0.002**

CFR (DM)

before | 1 hour
---|---
3.1±1.1 | 2.2±0.7

**p=0.0001**

CFR (IGT)

before | 1 hour
---|---
3.0±0.8 | 2.6±0.6

**p<0.0001**
Comparison of CFR among all groups

(before glucose loading)

(1 hour after glucose loading)
Comparison of c-CFR between all groups

p=0.006

p=0.03

p=NS

<table>
<thead>
<tr>
<th>Group</th>
<th>c-CFR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>-13±16</td>
</tr>
<tr>
<td>IGT</td>
<td>-22±7</td>
</tr>
<tr>
<td>DM</td>
<td>-26±10</td>
</tr>
</tbody>
</table>
Correlation between total insulin, HOMA-R and c-CFR in N group

Total insulin means the sum of serum insulin concentration before and 1 hour, 2 hour after glucose loading.
Summary

- Acute hyperglycemia attenuated CFR in all groups.
- C-CFR was significantly greater in the IGT and DM groups than in the N group.
- In the IGT and DM groups, a decline of CFR after glucose load was mainly caused by a reduction of coronary flow velocity at the hyperemia. On the other hand, a decline of CFR after glucose load was mainly caused by an increase of coronary flow velocity at the baseline in the N group.
- C-CFR had a significant negative correlation with the sum of insulin concentration and HOMA-R in the N group.
Conclusions

Acute hyperglycemia attenuated CFR in not only DM but also IGT/Normal group; indicating coronary microcirculation maybe injured even in the early stage of glucose intolerance.

The hyper-insulinemia / insulin resistance may play some role in such a microcirculatory impairment.