Pharmacodynamics and pharmacokinetics of nifedipine in patients with congestive heart failure

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Abstract Twenty-seven cases of congestive heart failure (CHF) were treated with nifedipine (Nif) 20 mg po. Significant improvements in resting hemodynamics were found in 22 cases. The higher the basal systemic vascular resistance (SVR) and pulmonary artery end diastolic pressure (PAEDP) were, the greater the magnitudes of reduction found (r = 0.84 and 0.77, P <0.01, respectively). Exercise hemodynamics investigation showed that Nif led to a lowering of SVR, PAEDP and pulmonary vascular resistance (PVR), with increases in SV and concentration of 5-10 ng/ml with a maximum being observed at the concentration of 20 ng/ml. No further vasodilatation was found when the plasma concentration exceeded 20 ng/ml. No remarkable deviations from the normal ranges of Nif pharmacokinetics were found in CHF patients. The plasma norepinephrine level decreased markedly 2 and 7h after Nif. Thus, it is concluded that oral Nif is beneficial in severe CHF patients having low cardiac output and high SVR.

Key words pharmacokinetics: pharmacodynamics: nifedipine: congestive heart failure: vascular resistance: norepinephrine

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Nifedipine (Nif) 20 mg po treatment 27 cases of CHF patients; 30 day admission; heart rate 65/min, MAP of 70/50 mmHg, beats of 130/min. Three patients with CHF-A and 3 patients with CHF-C in severe congestive heart failure. After treatment with Nifedipine, the systolic blood pressure increased moderately and diastolic blood pressure decreased. Nifedipine can be an effective treatment for congestive heart failure.
Methods

**Nifedipine** (nifedipine, NF) is widely used for the treatment of hypertension, angina pectoris, and other cardiovascular diseases. It is known for its potent vascular smooth muscle relaxing effects. However, its therapeutic effects are not clear-cut, and the risk of adverse reactions cannot be ignored.

NF was identified in a recent study as a potential therapeutic agent for hypertension. The study was conducted on a group of patients with essential hypertension, and the results showed a significant reduction in blood pressure and an improvement in systemic vascular resistance.

**Calcium Blockers**

Calcium blockers are a class of drugs that reduce the amount of calcium entering the heart and blood vessels. This reduces the force of heart contractions and the rate of blood flow, which can lower blood pressure and reduce the workload on the heart.

**The Effect of Nifedipine on Blood Pressure**

A study by Dr. Smith et al. published in the Journal of Hypertension found that patients taking nifedipine had a significant decrease in systolic and diastolic blood pressure compared to the control group. The study also showed that nifedipine was well tolerated by patients and had a low incidence of adverse effects.

**Conclusion**

In conclusion, the use of nifedipine as a therapeutic agent for hypertension shows promise. Further research is needed to fully understand its mechanisms of action and to develop optimized treatment regimens for patients.
**Null Hypothesis:**

- **Statistical Analysis:**
  - Use appropriate statistical tests for comparing the groups.
  - Include effect sizes and confidence intervals where applicable.

**Results:**

-⽤药后 2 h，HR 为 80 次/分，CI 为 3.0 L/min/m²，SVO2 为 65%。
- 用药后 2 h，CI 显著增加（P < 0.05），SVO2 未见变化。

**Discussion:**

- HR 和 CI 的变化可能反映了心率和心输出量的响应。
- SVO2 的增加可能与氧供的改善有关。

**Conclusion:**

- 尽管 HR 和 CI 有所增加，但 SVO2 未见明显变化，可能暗示此药物对改善全身氧供的作用有限。

**References:**

- 参考文献列表，包括相关文献的引用。

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**Table 1:**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>HR (bpm)</th>
<th>mBP (mmHg)</th>
<th>PAEDP (mmHg)</th>
<th>CI (L/min/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>12</td>
<td>95</td>
<td>4.5</td>
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<tr>
<td>2</td>
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<tr>
<td>8</td>
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<td>24</td>
<td>75</td>
<td>3.3</td>
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</tbody>
</table>

**After no nitridipine 20 mg**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>HR (bpm)</th>
<th>mBP (mmHg)</th>
<th>PAEDP (mmHg)</th>
<th>CI (L/min/m²)</th>
</tr>
</thead>
<tbody>
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<td>24</td>
<td>75</td>
<td>3.3</td>
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</tbody>
</table>

**Baseline**

- HR: 120 bpm
- mBP: 160 mmHg
- PAEDP: 120 mmHg
- CI: 4.5 L/min/m²

**after no nitridipine 20 mg**

- HR: 120 bpm
- mBP: 160 mmHg
- PAEDP: 120 mmHg
- CI: 4.5 L/min/m²
运动血流动力学变化

CHF病人运动时心率增加（99±27增加至116±26bpm，P<0.05）。

MBP增加（14.4±2.6增加至15.3±2.8kPa，P<0.01），PAEP明显增加（3.6±1.1增加至4.1±1.1kPa，P<0.01），SVR下降（0.019±0.005降低至0.014±0.004N·m·s·cm⁻²，P<0.01），CI增加（2.8±1.1增加至3.9±1.2L·min⁻¹·m⁻²，P<0.01），Nif明显改善病人运动后血流动力学，均因试验表明。Nif使运动后

血流动力学变化

10名正常人服Nif前及服后2，7h，血流NE含量分别为106±94，111±65，98±53pg/ml，服后NE无变化（P>0.05）。12例CHF病人服Nif前血流NE明显增高，可达738±361pg/ml，服药后2h降低至506±147pg/ml，P<0.05，7h后维持较低水平为539±153pg/ml（P<0.05）。
### Tab 2. Effect of nifedipine on exercise hemodynamics in patients with congestive heart failure.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Baseline exercise</th>
<th>Nifedipine</th>
<th>Nifedipine exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>95 ± 27</td>
<td>116 ± 58**</td>
<td>95 ± 24</td>
<td>117 ± 25**</td>
</tr>
<tr>
<td>mBP (KPa)</td>
<td>14 ± 2.6</td>
<td>15 ± 2.1**</td>
<td>11 ± 1.8</td>
<td>12 ± 1.1**</td>
</tr>
<tr>
<td>PAPDP (KPa)</td>
<td>3.2 ± 1.3</td>
<td>6.3 ± 1.3**</td>
<td>2.3 ± 1.9</td>
<td>3.3 ± 1.8**</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>1.4 ± 0.7</td>
<td>6.1 ± 1.8**</td>
<td>4.9 ± 1.1</td>
<td>7.1 ± 2.7**</td>
</tr>
<tr>
<td>CI (L/min·m²)</td>
<td>2.8 ± 1.1</td>
<td>3.8 ± 1.3**</td>
<td>3.9 ± 0.6</td>
<td>4.2 ± 1.0**</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>44 ± 12</td>
<td>57 ± 11**</td>
<td>50 ± 17</td>
<td>50 ± 17</td>
</tr>
<tr>
<td>SVI (ml/m²)</td>
<td>23 ± 7</td>
<td>31 ± 10**</td>
<td>33 ± 18</td>
<td>40 ± 9**</td>
</tr>
<tr>
<td>SVR (N·m·cm⁻³⁻¹)</td>
<td>0.109 ± 0.005</td>
<td>0.014 ± 0.004**</td>
<td>0.012 ± 0.006</td>
<td>0.012 ± 0.006**</td>
</tr>
<tr>
<td>PVR (N·m·cm⁻³⁻¹)</td>
<td>0.009 ± 0.002</td>
<td>0.006 ± 0.002*</td>
<td>0.004 ± 0.000</td>
<td>0.004 ± 0.000*</td>
</tr>
</tbody>
</table>

### Tab 3. Comparison of nifedipine pharmacokinetics between normal volunteers and patients of congestive heart failure.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Volunteers (n = 5)</th>
<th>Patients (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AU (mg·h·ml⁻¹)</td>
<td>37 ± 185</td>
<td>353 ± 217</td>
</tr>
<tr>
<td>T₁/₂ (h)</td>
<td>3.2 ± 1.6</td>
<td>5.5 ± 2.4</td>
</tr>
<tr>
<td>T₉₀ (h)</td>
<td>4.2 ± 1.2</td>
<td>3.6 ± 2.4</td>
</tr>
<tr>
<td>Cmax (mg/ml)</td>
<td>32 ± 6</td>
<td>31 ± 4.9</td>
</tr>
<tr>
<td>T₉₀ (h)</td>
<td>0.4 ± 0.7</td>
<td>0.7 ± 0.4</td>
</tr>
</tbody>
</table>

### Fig 4. Plasma nifedipine concentration after po nifedipine 25 mg in normal volunteers (n = 10) and the patients of congestive heart failure (n = 12). (○)

### Discussion

我们首先在国内建立了高效液相色谱条件，进行了样品检测血内 Nif 代谢的种方法，方法简便，结果稳定，但在实际工作中发现 Nif 在 5-10 mg/ml 时，就有效扩张作用，本法灵敏度为 5 mg/ml，误差略高，本实验将在继续进行条件优化

本实验未能观察到 CHF 可能引起的药物代谢的变化，可能主要原因是药物代谢个体差异大、Kleinbloesem 等报告 58 例 CKF 患者，AUC 从 100 mg·h·ml 至 800 mg·h·ml 不等。本实验观察 CHF 患者 AUC

## 学术背景

### 3.1.1 Nifedipine Therapy

Nifedipine is a calcium channel blocker that is used to treat coronary heart disease and hypertension. It is a member of the dihydropyridine class of calcium channel blockers. Nifedipine is available in both oral and injectable forms. It acts by blocking calcium ions from entering the smooth muscle cells of blood vessels, which relaxes the muscles and decreases blood pressure. In patients with CHF, nifedipine may be used to reduce angina and improve exercise tolerance. Nifedipine is not recommended for the treatment of heart failure because it may increase the risk of arrhythmias.

### 3.1.2 Clinical Use

Nifedipine is primarily used to treat angina pectoris, hypertension, and peripheral arterial disease. It is also used to treat Raynaud's disease, which is a condition that affects the arteries in the fingers and toes, causing them to become pale and numb. In the treatment of angina, nifedipine may be used alone or in combination with other medications such as beta-blockers. In the treatment of hypertension, nifedipine may be used alone or in combination with other antihypertensive medications.

### 3.1.3 Pharmacokinetics

Nifedipine is rapidly absorbed following oral administration and peak plasma concentrations are typically achieved within 1-2 hours. The extent of absorption is reduced with food, and therefore, the drug should be taken with a glass of water on an empty stomach. Nifedipine is extensively metabolized in the liver and the primary metabolites are excreted in the urine. The elimination half-life of nifedipine is approximately 2-4 hours.
References


