Evolution of infarct size during the early use of nifedipine in patients with acute myocardial infarction: The Norwegian Nifedipine Multicenter Trial

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ABSTRACT In a multicenter double-blind study, 227 patients with suspected acute myocardial infarction (AMI) were randomized within 12 hr from onset of symptoms to treatment with nifedipine (112 patients) or placebo (115 patients). AMI was confirmed in 74 patients on nifedipine and in 83 on placebo. Patients with AMI received nifedipine 5.5 ± 2.9 hr (mean ± SD) after onset of symptoms. Infarct size was assessed by the release of creatine kinase isoenzyme MB (CK-MB). Infarct size index (CK-MB g eq/m²) was 25 ± 16 (n = 71) in the nifedipine group and 23 ± 13 (n = 77) in the placebo group (NS). After the first 10 mg of nifedipine systolic blood pressure fell from 147 ± 30 to 135 ± 28 mm Hg (p < .01) and heart rate rose from 75 ± 18 to 79 ± 19 beats/min (p < .01). No change was observed after the first placebo dose. The treatment was continued for 6 weeks. Over this period there were 10 deaths in each group. Early treatment with nifedipine in patients with AMI does not seem to reduce infarct size as determined by enzyme level.


THE CALCIUM ANTAGONIST nifedipine has been shown during the last decade to be effective in the treatment of angina pectoris and more recently in the treatment of hypertension and heart failure. A cardioprotective effect of nifedipine has also been demonstrated after experimental coronary occlusion. There are several reasons why nifedipine might limit myocardial damage in patients with acute myocardial infarction (AMI). By reducing systemic vascular resistance, nifedipine might improve left ventricular unloading and reduce left ventricular workload. Dilatation of coronary arteries might enhance collateral flow to the ischemic region and possibly restore blood flow in situations in which spasm contributes to the ischemia. Furthermore, nifedipine might inhibit detrimental cellular uptake of Ca++ during ischemia.

This trial was primarily designed to investigate whether early intervention with nifedipine in AMI might reduce infarct size, as determined enzymatically by measurement of creatine kinase isoenzyme MB (CK-MB) levels. The amount of increase in serum level of this enzyme has been shown to have a close relationship to infarct size.

Methods

Patient selection and recruitment. All patients who were admitted to the four participating hospitals with suspected AMI during the trial period (885 patients) were screened for inclusion. Inclusion criteria were (1) severe central chest pain for at least 30 min, continuing on admission or until an analgesic was given, or (2) electrocardiographic changes suggesting an AMI (not previously recognized ST segment elevation >0.2 mV in precordial leads or >0.1 mV in extremity leads, or a Q wave ≥0.04 sec that had not been previously recognized). These inclusion criteria were fulfilled by 623 patients, 396 (64%) of whom were excluded (table 1).

Allocation and treatment. After informed consent was obtained, eligible patients of both sexes were randomly assigned to treatment with either nifedipine (10 mg capsules) or placebo. Patients at each center were assigned in blocks of 10 and given capsules from prenumbered bottles. A patient was considered to be included in the trial when he or she took the first capsule sublingually. Subsequent doses were 10 mg orally and were begun 30 min after the first dose unless systolic blood pressure was below 90 mm Hg. For the first 2 days 10 mg was given five
TABLE 1
Selection of patients for participation in the study

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>All patients (n)</th>
<th>AMI patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened for possible entry</td>
<td>885</td>
<td>417</td>
</tr>
<tr>
<td>Absence of inclusion criteria</td>
<td>262</td>
<td>45</td>
</tr>
<tr>
<td>Reasons for exclusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;35, ≥75 years</td>
<td>151</td>
<td>87</td>
</tr>
<tr>
<td>Evaluation ≥12 hr after onset</td>
<td>105</td>
<td>60</td>
</tr>
<tr>
<td>Use of calcium antagonist within last 48 hr</td>
<td>45</td>
<td>16</td>
</tr>
<tr>
<td>Other serious disease</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>Death before inclusion, hypotension, pulmonary edema, aortic, or mitral stenosis</td>
<td>24</td>
<td>16</td>
</tr>
<tr>
<td>Refusal to participate</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Inability to attend 6 week follow-up</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Other reasons</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Randomly assigned treatment</td>
<td>227</td>
<td>159</td>
</tr>
</tbody>
</table>

THERAPY AND PREVENTION—MYOCARDIAL INFARCTION

Estimation of sample size. The study was designed so that there would be a 90% chance of detecting a 30% reduction in infarct size by nifedipine. The probability of obtaining a false-positive result was 5%. Determination of infarct size was the primary end point of the trial. The coefficient of variation for infarct size was estimated to be about 50% so that about 120 patients with infarcts of calculable size were required. However, to allow for patients who might be found not to have AMI and for patients whose infarct size could not be calculated, the goal for recruitment was set at 230 patients.

Analysis of results. Classification of infarct size (A to C), infarct sites, Kd determinations, and causes of death was done blindly with respect to treatment group. Data were analyzed by the study coordinator (P. A. S.). Mortality was analyzed with a life table method. Continuous variables were reported as mean ± SD, unless otherwise stated. Standard textbook methods (parametric and nonparametric) were used as appropriate for the comparison of treatment effects. All statistical methods were based on two-sided tests, and p less than .05 was considered the level of significance.

Results

Trial population. Of the 227 patients who were randomly assigned treatment, 112 received nifedipine and 115 placebo. In five patients, two of whom received nifedipine, the protocol was violated; one had been receiving verapamil and in four the start of treatment was more than 12 hr after onset of symptoms. Of these five patients, one nifedipine and one placebo patient developed AMI.

Of the remaining 222 patients, the diagnosis of AMI (class A or B) was confirmed in 74 (67%) of 110 nifedipine patients and 83 (74%) of 112 placebo patients. In the population as a whole treatment was initiated a mean 5.2 ± 3.0 hr after onset of symptoms, with a median value of 4 hr and 10 min. However, nifedipine patients with AMI were included slightly later than placebo patients with AMI (5.48 ± 2.86 vs 4.62 ± 2.80 hr after onset of symptoms in the nifedipine and placebo groups, respectively; t = 1.9, p = .059). Other baseline characteristics are listed in table 2. No baseline differences were significant at p < .05.

Mortality and adverse reactions. Mortality at 6 weeks was nearly identical in the two groups; 10 of 112 nifedipine patients and 10 of 115 placebo patients died. The life table graph is shown in figure 1. All deaths occurred in patients who had developed an AMI. There were six deaths from cardiac failure and four sudden deaths in each group.

Untoward effects possibly related to the treatment was noted in 64 (28%) of the 227 randomized patients. There were 32 patients with adverse reactions in each group. Most reactions were classified as mild, although nine patients in the nifedipine group and six patients in the placebo group had to be withdrawn from treatment because of suspected adverse reactions (NS) (table 3).
TABLE 2
Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>AMI patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N P</td>
<td>N P</td>
</tr>
<tr>
<td></td>
<td>(n = 110)</td>
<td>(n = 74)</td>
</tr>
<tr>
<td></td>
<td>(n = 112)</td>
<td>(n = 83)</td>
</tr>
<tr>
<td>Women (%)</td>
<td>23 29</td>
<td>18 22</td>
</tr>
<tr>
<td>Previous AMI (%)</td>
<td>28 34</td>
<td>26 35</td>
</tr>
<tr>
<td>Previous angina (%)</td>
<td>60 53</td>
<td>50 49</td>
</tr>
<tr>
<td>Rales &lt;½ lung field on entry (%)</td>
<td>27 29</td>
<td>24 25</td>
</tr>
<tr>
<td>Rales ≥½ lung field on entry (%)</td>
<td>8 13</td>
<td>8 16</td>
</tr>
<tr>
<td>ST segment elevation on entry (%)</td>
<td>49 54</td>
<td>51 55</td>
</tr>
<tr>
<td>New Q wave on entry (%)</td>
<td>19 22</td>
<td>24 28</td>
</tr>
<tr>
<td>Long-term use of β-receptor blockade (%)</td>
<td>18 24</td>
<td>14 22</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>61 ± 6</td>
<td>61 ± 8</td>
</tr>
<tr>
<td></td>
<td>61 ± 9</td>
<td>60 ± 9</td>
</tr>
<tr>
<td>Hours from onset to study entry</td>
<td>5.4 ± 3.0</td>
<td>5.5 ± 2.9</td>
</tr>
<tr>
<td></td>
<td>4.9 ± 2.9</td>
<td>4.6 ± 2.8</td>
</tr>
<tr>
<td>First CK-MB level (IU/l)</td>
<td>29 ± 33</td>
<td>35 ± 38</td>
</tr>
<tr>
<td></td>
<td>26 ± 41</td>
<td>31 ± 47</td>
</tr>
</tbody>
</table>

None of the differences listed above reached significance at <.05 (chi-square or student’s t test).

N = nifedipine; P = placebo.

^Mean ± SD.

Enzyme analysis. Class A myocardial infarction (see Methods) was diagnosed in 67 of 110 nifedipine patients and in 76 of 112 placebo patients (NS) and class B myocardial infarction was diagnosed in seven patients in each treatment group.

The calculation of accumulated CK-MB release was impossible in three nifedipine and in six placebo patients because of death before the peak CK-MB level was reached or an insufficient number of CK-MB samples.

The distribution of the times from onset of symptoms until peak CK-MB level was reached is shown in figure 2. The mean values were 22.5 ± 14.9 hr in the nifedipine group vs 22.1 ± 9.4 hr in the placebo group (NS). Peak CK-MB level was reached before 20 hr in 46% of nifedipine patients and in 38% of placebo patients (NS). Kds could be calculated from the declining part of the CK-MB curve in 60 patients in each group and were nearly identical (nifedipine group, 0.0485 ± 0.0122/hr; placebo group, 0.0487 ± 0.0111/hr; NS). A common Kd value of 0.0486/hr was used for 11 nifedipine and in 17 placebo patients.

The evolution of the CK-MB release in the two groups is illustrated in figure 3. Although patients in the nifedipine group generally had larger mean CK-MB values than those in the placebo group more than 16 hr after onset, this difference did not reach statistical significance. Calculated infarct size index (ISI; CK-MB geq/m²) was 25 ± 16 (range 1 to 61.3) in the nifedipine group and 23 ± 13 (range 1.2 to 51.2) in the placebo group (NS). The distribution of ISIs is shown in figure 4. The ISIs of some subgroups are listed in table 4. Subgroups of patients in the nifedipine group with initial systolic hypertension or with a tachycardia.

![FIGURE 1. Life table of survival for all patients randomly assigned to treatment.](http://circ.ahajournals.org/)

![FIGURE 2. Distribution of times from onset of symptoms to peak CK-MB.](http://circ.ahajournals.org/)

![FIGURE 3. Distribution of total number of adverse reactions recorded in 32 nifedipine and 32 placebo patients.](http://circ.ahajournals.org/)
FIGURE 3. The evolution of CK-MB release. Values are mean ± SEM. Statistically significant (p < .05) differences between the two groups could not be demonstrated at any time. Points on individual release curves were interpolated to give release values at the hours marked on the abscissa if a blood sample was taken outside the marked hours ± 5 min.

diagnostic or hypotensive response to the treatment showed a
tendency towards larger ISIs.

Clinical parameters. After the first dose of nifedipine
mean systolic blood pressure decreased from 147 ± 30
to 135 ± 28 mm Hg (p < .01), but it did not change
after the first placebo dose (table 5). There was a
Corresponding increase in heart rate from 75 ± 18 to
79 ± 19 beats/min (p < .01) vs no change in the
placebo group. These differences were also apparent
after the later doses, but at discharge from hospital
there were no significant differences between the two
groups with respect to heart rate or blood pressure
(table 6).

An initial systolic blood pressure of 160 mm Hg or
more was recorded in 30 nifedipine and 27 placebo
patients with AMI. After two doses the systolic blood
pressure had declined from 174 ± 21 to 144 ± 22 mm
Hg in hypertensive patients on nifedipine, and from
175 ± 18 to 162 ± 26 mm Hg in hypertensive patients
on placebo (p < .01 for nifedipine compared with
placebo patients). In patients with AMI a systolic
blood pressure less than 90 mm Hg after the first two
doses was noted in 29% of nifedipine-treated vs 18%
of placebo-treated patients (NS).

The rate of occurrence of serious arrhythmias and
conduction defects was similar in the two groups.
There were no significant differences in the prevalence
of reported angina pectoris or heart failure at discharge.
Morphine requirements were similar in the two
groups, but the mean dosage of furosemide necessary
in the first 4 days was significantly larger for the place-
bo group (99 ± 167 vs 49 ± 113 mg in the nifedipine
group; p < .05) (table 6).

Effects of exclusions. Data from one patient on nifedipine
and one on placebo with AMI were excluded from
the analysis because of protocol violation before entry.
Inclusion of these data does not change the mean values
given previously.

Infarct size was not calculable in three patients re-
ceiving nifedipine and in six on placebo. If these pa-

table 4

<table>
<thead>
<tr>
<th></th>
<th>Nifedipine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>n=71, Mean ± SD</td>
<td>n=77, Mean ± SD</td>
</tr>
<tr>
<td>Class A AMI</td>
<td>64, 27±15</td>
<td>70, 25±13</td>
</tr>
<tr>
<td>No previous AMI</td>
<td>29, 28±15</td>
<td>33, 22±12</td>
</tr>
<tr>
<td>Chronic β-receptor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>blockade</td>
<td>9, 24±10</td>
<td>17, 20±10</td>
</tr>
<tr>
<td>Entry CK-MB &lt;40 IU/l</td>
<td>51, 25±16</td>
<td>63, 23±13</td>
</tr>
<tr>
<td>Entry SBP &gt;160 mm Hg</td>
<td>28, 28±17</td>
<td>23, 18±13</td>
</tr>
<tr>
<td>Fall in SBP of &gt;10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>to levels of &lt;90 mm Hg</td>
<td>50, 25±15</td>
<td>31, 19±10</td>
</tr>
<tr>
<td>Increase in heart rate &gt;10 bpm</td>
<td>21, 32±15</td>
<td>20, 23±13</td>
</tr>
<tr>
<td>Transmural infarctions</td>
<td>57, 29±15</td>
<td>62, 26±12</td>
</tr>
<tr>
<td>Nontransmural infarctions</td>
<td>14, 9±9</td>
<td>15, 11±8</td>
</tr>
<tr>
<td>Anterior infarctions</td>
<td>22, 30±17</td>
<td>24, 24±12</td>
</tr>
<tr>
<td>Inferior infarctions</td>
<td>37, 27±12</td>
<td>36, 27±11</td>
</tr>
<tr>
<td>Other or undetermined infarct location</td>
<td>12, 9±8</td>
<td>17, 13±11</td>
</tr>
<tr>
<td>Treated ≤3 hr after onset</td>
<td>20, 31±15</td>
<td>27, 23±13</td>
</tr>
<tr>
<td>Treated &gt;3, ≤6 hr after onset</td>
<td>27, 24±16</td>
<td>31, 26±13</td>
</tr>
<tr>
<td>Treated &gt;6 hr after onset</td>
<td>24, 21±13</td>
<td>19, 18±11</td>
</tr>
</tbody>
</table>

Class A AMI = peak CK-MB >50 IU/liter and a typical serum curve; AP = angina pectoris; SBP = systolic blood pressure.

*Infarct size was not calculable in one nifedipine patient and in five placebo patients with initial systolic blood pressures ≥160 mm Hg.
TABLE 5
Changes in blood pressure and heart rate

<table>
<thead>
<tr>
<th></th>
<th>Values recorded before:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose 1</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>147 ± 30</td>
</tr>
<tr>
<td>Placebo</td>
<td>144 ± 27</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>93 ± 17</td>
</tr>
<tr>
<td>Placebo</td>
<td>93 ± 11</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>75 ± 18</td>
</tr>
<tr>
<td>Placebo</td>
<td>77 ± 22</td>
</tr>
</tbody>
</table>

A p < .05 by paired t test compared with value before dose 1.

Patients are assigned an infarct size corresponding to the median ISI in the whole population (22 CK-MB geq/ m³), the mean ISIs are still 25 ± 16 in the nifedipine group and 23 ± 12 in the placebo group. If data from all randomly assigned patients are included into the analysis and those without AMI are given an infarct size value of zero, the mean ISI becomes 17 ± 18 for the nifedipine group and 17 ± 15 for the placebo group.

Discussion

The optimistic expectations that nifedipine therapy would reduce infarct size were not fulfilled in the present study. This might have been the result of methodologic problems, e.g., an inadequate sample size. A revised calculation of statistical power with the use of the mean and SD of the ISI in the placebo group reveals there was a probability of greater than 0.90 of detecting an infarct size reduction of 30% by nifedipine. However, the chance of having missed a 20% reduction was 0.37.

With respect to adverse reactions, it seems that nifedipine is reasonably well tolerated in patients with suspected AMI. The present study confirms previous reports of nifedipine as an efficacious antihypertensive agent. However, normalization of the blood pressure by nifedipine in the subgroup with initial hypertension was not associated with any reduction in infarct size. The results indicate that nifedipine was unable to reduce ischemic pain in patients with AMI. Reduced need for furosemide in the nifedipine-treated patients, in spite of a tendency to large enzyme values, may be an indication of a beneficial effect on heart failure. However, increased furosemide use in placebo patients may also be due to the higher proportion of patients with pulmonary rales on entry in this group (table 2).

The two groups were comparable with respect to baseline characteristics, but it is noteworthy that among patients with AMI β-receptor blockers were used before entry in only 13% of nifedipine patients compared with in 21% of placebo patients. Since β-receptor blockers may reduce infarct size,15 this might introduce a bias favoring the placebo group. The combination of β-receptor blocker and nifedipine was not associated with reduced infarct size in the present study, but the number of patients on this combination was too small to evaluate the efficacy of this combination for limitation of infarct size.

The mean delay from onset of symptoms to the initiation of treatment was 5.5 ± 2.9 hr in the nifedipine group. This delay may have been important since myocardial injury is believed to be irreversible after 4 to 6 hr of grave ischemia.16 However, there was no trend toward smaller ISI in the subgroup of 20 patients on nifedipine treated before 3 hr after onset of symptoms (table 4).

There have been some objections to the use of calculated enzyme release as an indicator of myocardial infarct size,17 but several studies have shown a good correlation with autopsy assessments.13,14,18 Since the measured Kd was nearly identical in the two groups, it is not likely that nifedipine had any influence on CK-MB degradation. Increased flow to the infarct area might possibly increase the proportion of enzyme that is washed out. Early reperfusion with streptokinase has been associated with earlier and higher CK-MB

TABLE 6
Clinical parameters and clinical events in patients with AMI

<table>
<thead>
<tr>
<th></th>
<th>Nifedipine (n = 74)</th>
<th>Placebo (n = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarction (%)</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>Inferior infarction (%)</td>
<td>54</td>
<td>45</td>
</tr>
<tr>
<td>Other or unclassifiable location (%)</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>Nontransmural infarction (%)</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Ventricular tachycardia (%)</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td>Ventricular fibrillation (%)</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Complete AV block or AV block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd degree, Mobitz II (%)</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Nonfatal reinfarction within 6 weeks (%)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Morphine dosage first 4 days (mg)A</td>
<td>42 ± 39</td>
<td>36 ± 33</td>
</tr>
<tr>
<td>Furosemide dosage first 4 days (mg)A</td>
<td>49 ± 113B</td>
<td>99 ± 167</td>
</tr>
<tr>
<td>Heart rate at discharge (bpm)A</td>
<td>73 ± 15</td>
<td>71 ± 12</td>
</tr>
<tr>
<td>Systolic blood pressure at discharge (mm Hg)A</td>
<td>126 ± 23</td>
<td>127 ± 20</td>
</tr>
<tr>
<td>Cardiac volume at discharge (ml/m²)A</td>
<td>502 ± 105</td>
<td>487 ± 122</td>
</tr>
</tbody>
</table>

A Mean ± SD.
B p < .05.
peaks, but the correlation between the enzymatic and histologic infarct size is apparently not greatly influenced unless reperfusion occurs very early (<2 hr) after the occlusion. There was a slight tendency towards earlier and higher peaks in the nifedipine group in the present study (figure 2), but this was not significantly different from that in the placebo group. Still, the possibility of increased washout of enzyme cannot be ruled out in the present trial.

The graph of the evolution of CK-MB release (figure 3) shows a general, but nonsignificant, trend toward larger infarct size in the nifedipine group. This trend was especially pronounced in some nifedipine subgroups (table 4) including those of patients with initial hypertension, patients with hypotension or a reduction in systolic blood pressure of more than 10%, and patients with an increase in heart rate of more than 10 beats/min after the first two doses. When tested individually with a rank-sum test, these differences are significant at p < .05, but caution should be exercised in claiming any significance of results of multiple retrospective subgroup analysis. One explanation for the increased ISI in some subgroups is that a chance predominance of patients with large infarctions in the nifedipine group would lead to an increased frequency of heart failure, with tachycardia and hypotension being the result, and not the cause, of large infarctions.

From the subgroup analysis in the present study it might be hypothesized that nifedipine increases infarct size in some patients. An increased heart rate could reduce coronary perfusion time and increase oxygen demands and hypotension might reduce coronary perfusion pressure and thereby coronary flow if the resistant vessels are maximally dilated. These effects of nifedipine might have outweighed its beneficial effects on collateral flow and resistance to ischemia. It is evident from the changes in heart rate and blood pressure observed that amounts of nifedipine sufficient to produce systemic hemodynamic changes were given in the present study. A higher dosage of nifedipine might have increased ischemia by reducing coronary perfusion pressure and inducing reflex tachycardia. Selwyn et al. found that large doses of nifedipine could increase myocardial injury in dogs and large doses of nifedipine have been shown to aggravate angina in some patients.

Another mechanism whereby nifedipine might have increased ischemia is by regional or transmural redistribution of coronary flow. Dilatation of resistant vessels in nonischemic or moderately ischemic myocardium might have produced a "steal" phenomenon in the presence of multiple flow-limiting proximal stenoses. The experimental evidence for a steal effect of nifedipine seems conflicting, but there are several reports of nifedipine-induced ischemia in humans. If the action of the drug is dependent on the presence of collaterals, limitation of infarct size most likely would be expected in patients with prior symptomatic coronary heart disease. Although the present study shows a slight tendency towards larger ISIs in patients without prior symptomatic coronary heart disease, this difference is not significant. The favorable effect of nifedipine on acute ischemic injury in experimental preparations may be due to a better collateral circulation in dogs than in humans; the findings in dogs could not be reproduced in species like the baboon with poorly developed collateral circulation, thus supporting results of the present study in humans.

Preliminary results from a study in which another calcium antagonist (verapamil) was used in patients with AMI are now available. In 1436 patients with AMI randomly assigned to verapamil or placebo, there was no effect of the drug on 6 month survival and infarct size was also similar in a subgroup of 100 patients in whom it was assessed by serial creatine kinase analysis. In a recent double-blind study, Mueller et al. investigated the effects of nifedipine in 191 patients with threatened or established AMI. Their dosage of nifedipine was larger than that in the present study, but the effects on infarct size and 6 month mortality were similar.

As yet, there is no reason to recommend general treatment with calcium antagonists to reduce infarct size.

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