Nifedipine and Angina Pectoris*

Short-Term Changes in Quantitative Coronary Angiography with Nifedipine and Clinical Response to Treatment in Effort-Induced, Mixed, and Spontaneous Angina Pectoris

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Changes induced by nifedipine (10 mg sublingually) in the residual luminal diameter of significant (>50 percent) coronary lesions were assessed angiographically in 69 patients with effort-induced angina (group 1), in 22 patients with mixed angina (group 2), and in 14 patients with Prinzmetal's angina (group 3). These changes were related to the clinical response to treatment with the same drug, as evaluated through diary records and Holter monitoring in the mixed (spontaneous component) and Prinzmetal forms and through exercise testing in effort-induced and mixed (effort-associated component) angina. In groups 1 and 2, segments of stenotic vessels showed either an increase or decrease or no change in diameter with the calcium antagonist; in group 3, the majority of the lesions had compliant portions which invariably responded with dilatation. Nifedipine failed to improve cases with exertional (20 percent [14/69] unchanged; 19 percent [13/69] worsened) and mixed (41 percent [9/22] exacerbated) forms; 100 percent of the 14 patients with the Prinzmetal form had relief of the anginal episodes. In group 1, the response to exercise tests was dissociated from the short-term vasomotor pattern, and the pressure-rate product failed to explain the clinical results. Forty-five percent (ten) of the patients in group 2 showed significant short-term widening of critical stenoses, as well as obvious improvement; patients who did worse with treatment in this group had reacted to nifedipine with narrowing of critical stenoses. These data suggest that the response to nifedipine of classic effort-induced angina is probably the net result of an interaction of changes in myocardial oxygen consumption and supply; coronary vasomotion has a role in mixed angina, and influences of nifedipine may be either favorable or unfavorable; stenotic lesions in the Prinzmetal form are quite sensitive to the relaxant action of calcium blockade, and this probably represents a background to the highly positive clinical response to treatment.

In the morphologic spectrum of human coronary artery stenosis, 74 percent of the sections narrowed by atherosclerosis have an eccentric residual lumen which is partially circumscribed by an arc of normal arterial wall.1 This provides a mechanism whereby intraluminal pressure and vasomotor tone variations may affect the luminal diameter and the resistance to flow.2 Clinical observations also suggest that an increase in large epicardial coronary arterial tone, when superimposed on a preexisting coronary stenosis, may trigger or exacerbate myocardial ischemia. Thus, the concept has been supported that the pathogenesis of angina pectoris is based on fixed and dynamic obstruction of a coronary artery.2,4

The mechanisms of the antianginal action of nifedipine may include the following: (1) dilatation of the coronary arterioles and shunting of flow favoring ischemic subendocardial layers; (2) dilatation of the epicardial vessels and relief of coronary arterial spasm;5–11 (3) afterload reduction due to peripheral vasodilatation;12 and (4) negatively inotropic effect and alteration of the diastolic properties of the myocardium.13 Combinations and net consequences of these effects seem to underlie the therapeutic efficacy of nifedipine14 in patients with angina due to coronary vasoospasm, fixed obstruction, or both. Stone et al15 observed that the addition of nifedipine to conventional therapy was more effective in patients with documented vasoospasm than in those with classic exertional angina; frequency of angina also increased with nifedipine by 14 percent of the cases in the former and by 29 percent in the latter population. Cases in which nifedipine was associated with deterioration of the patients' clinical condition have been described by several authors.16–19 The reasons for these paradoxical responses are unknown.

This study was designed to characterize the short-

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term angiographic effects of nifedipine in different forms of angina and to seek a correlation with the clinical results which might provide guidelines for treatment.

**Materials and Methods**

**Patients**

Among 660 consecutive patients with angina who underwent coronary arteriography in our institution during the last 18 months, we selected those who presented the classic pattern of effort-induced angina (group 1; 69 patients) or of mixed angina (group 2; 22 patients), or of Prinzmetal's angina (group 3, 14 patients). The type and severity of the disease were evaluated in the untreated state through diary records and Holter monitoring in the mixed (spontaneous component) and Prinzmetal forms and through exercise testing in effort-induced and mixed (effort-associated component) angina. The same tests were used to assess the response to treatment. Patients were considered as having the classic effort-induced form if angina was provoked only by a stable consistent and predictable exertional threshold, without pain or ST-segment shift at rest, or ST-segment elevation during episodes of exertional pain; those subjects who exhibited a recognizable threshold of exertion for the development of angina who, additionally, experienced some episodes at rest were considered as having a mixed form, and finally, cases showing repetitive unequivocal ST-segment elevation at rest, associated or not with pain, with negative effort test, were classified as having Prinzmetal's angina. The following additional criteria for inclusion were satisfied: informed consent to participate in the investigation; age not exceeding 65 years; no treatment with nifedipine in the past; no history or signs of previous myocardial infarction, diabetes, cerebrovascular disease, valvular or primary myocardial diseases, or high blood pressure; no evident deterioration with tapering and discontinuation of the previous therapy; electrocardiographic documentation in groups 2 and 3 of at least one and three episodes of ST-segment shift per 24 hours, respectively, during the period with placebo; presence of sinus rhythm; no administration of nitrates within four hours of catheterization; absence of 50 percent or greater stenosis of the left main coronary artery; high-quality angiographic documentation of 50 percent or greater reduction in diameter (significant stenosis) at one site of the circumflex or left anterior descending or right coronary artery (or any combination of the three); and no sign of complete occlusion of one or more of the three major epicardial vessels. In group 3, two patients showed normal coronary arteriograms.

In addition to sublingual therapy with nitroglycerin, 61 patients were receiving β-adrenergic blocking drugs alone (29 patients) or in combination with long-acting nitrates (11 patients) or with calcium antagonists (11 patients) or all three agents (ten patients), 17 patients were receiving long-acting nitrates alone (14 patients) or combined with calcium antagonists (three patients), and 23 patients were receiving calcium antagonists (verapamil or diltiazem) alone. Twenty patients were not receiving any maintenance antianginal therapy.

**Design of Study**

The protocol shown in Figure 1 was used for the study and was approved by the local ethical committee. Once previous treatment had been discontinued and screening exercise tests had been carried out, patients were given a placebo for one week. For safety, we decided to restrict the use of placebo through the duration of the control Holter monitoring in those patients in group 3 who had more than ten episodes of angina in the 24 hours (four cases); however, in these cases, angina was not exacerbated by discontinuation of the previous therapy. At the end of the run-in, 48-hour Holter monitoring was performed, the basal evaluations were repeated, and coronary arteriography was carried out before and after a 10-mg dose of nifedipine was administered sublingually. Then patients entered the period of active treatment, consisting of two 72-hour single-blind phases during which nifedipine was given orally at dosages of 10 and 20 mg four times daily, respectively. Anginal attacks and adverse effects were recorded in a diary. At the end of each phase of treatment, patients again underwent clinical, Holter, and exercise evaluations. The response to treatment was assessed by exercise testing for effort-induced angina and the effort-associated component of mixed angina and by diary records and Holter monitoring for Prinzmetal's angina and the spontaneous component of the mixed form.

**Exercise Testing**

Exercise tests were performed in the postabsorptive state, 90 minutes after the last dose of medication, at approximately the same time each day, according to the Kaltenbach protocol. Patients were exercised upright on an isokinetic bicycle ergometer (Collins). The electrocardiogram was monitored continuously, and the standard

<table>
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<th>1 week</th>
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<tr>
<td>Taper and cease</td>
<td>S8</td>
<td>S8</td>
<td>S8</td>
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<tr>
<td>previous treatment</td>
<td>Placebo</td>
<td>Nifedipine</td>
<td>Nifedipine</td>
</tr>
</tbody>
</table>

CONTROL EVAL.*

CONTROL EVAL.*

PHASE 1 EVAL.*

PHASE 2 EVAL.*

CORON.ANGIO.*

* Evaluations

- Clinical evaluation
- N. of anginal attacks (diary)
- Graded bicycle exercise testing

△ Coronary angiography before and after nifedipine (10 mg s.i.)

□ 48 hours ambulatory Holter monitoring

Figure 1. Protocol of study. Placebo and nifedipine were given in single-blind (SB) fashion.
limb leads and leads V₁ to V₆ were recorded initially and after each minute of exercise. Blood pressure was measured each minute by cuff manometry, and heart rate was averaged from five consecutive beats. The rate-pressure product (double product) was calculated as the product of systolic blood pressure times heart rate. Exercise began at 150 kpm/min (25 W), and the workload was increased by 150 kpm/min every two minutes. For the initial evaluation with placebo, exercise was continued to the workload at which the patient indicated moderate angina or fatigue or until an ischemic ST-segment depression of 3 mm was induced in lead 2 or V₁ or V₆. The reproducibility of ST-segment depression was assured in a second control test carried out at the end of the period with placebo. Subsequent studies with nifedipine were performed to the maximal workload achieved in the evaluation with placebo. The ST-segment depression was manually measured and averaged from five consecutive beats in leads 2, V₁, and V₆ during all minutes of exercise and five minutes of recovery, so that the mean ST-segment depression could be obtained.

Holter Monitoring

Ambulatory electrocardiographic responses were evaluated from a calibrated two-channel recording made during the last 48 hours of the placebo and treatment periods. Two bipolar leads were chosen for monitoring, based upon leads showing ST-segment shifts in standard 12-lead ECGs performed during angina, either at rest (groups 2 and 3) or during exertion (group 1). These leads corresponded to V₁ or V₆ or V₃ or lead 2. The recorders used (Del Mar Avionics Electrocardiorders model 445) had a frequency response between 0.05 and 100 Hz. Patients kept an additional diary noting time of symptoms and activities; they were instructed to press the event marker button whenever attacks of angina occurred. An ischemic episode was defined as ST-segment depression or elevation of at least 1 mm from baseline for more than one minute.

Quantitative Angiography

Coronary cineangiograms were obtained by the Judkins technique in multiple projections, including cranial angulation, obtained in two views 90° apart (using Siemens-Elema equipment with C-arm), so that the patient was not moved during the study. Contrast medium (76 percent meglumine diatrizoate [Urografin]) was injected at a flow rate of 3 m/s. Angiograms were performed under constant conditions before and 25 minutes after a 10-mg sublingual dose of nifedipine, at the time at which a known hemodynamic effect (ie, decrease in aortic pressure) had occurred. Aortic pressure and heart rate were monitored continuously. Twelve coronary segments were analyzed from the first contrast injection into an artery and again from an injection repeated 15 minutes later in the same view. The normal luminal and minimal stenotic diameters before and after contrast medium were unchanged. Variations after nifedipine, therefore, could not be attributed to residual dilatation of large coronary arteries by contrast effects. Quantitative measurements were automated by a previously validated method of digital processing. Digital images were obtained by viewing each single-frame cineangiographic image with a television camera (RCA 1005 Vidicon), which served as input to a digital angiography system (ADAC 4100 C). The computerized analysis of the coronary normal luminal and stenotic diameters was obtained through an interactive computer program with previous magnification of the stenotic region and placement by the observer of two cursor points across the normal arterial diameter and the region of maximal coronary narrowing. This method provided the length of each diameter segment. The percentage of diameter stenosis was calculated as the diameter across the region of maximal narrowing divided by the diameter of the normal segment. Measurements were also performed at proximal, medial, and distal sites of normal coronary artery branches. In each patient, we analyzed one or more coronary lesions and selected those which were deemed to be in the distribution of ischemic ST-segment changes. Among the studied lesions, 58 percent were adequately visualized in the two projections, and measurements of the two perpendicular views were averaged; in the remaining lesions the measurements were made from a single angiographic view that was carefully repeated for the studies with the drug. A variation of 0.05 mm in the stenotic luminal diameter following nifedipine was taken as the threshold to define dilatation or constriction.

Data Analysis

Those performing analysis of exercise testing, Holter monitoring, and coronary angiograms were prevented from knowing which of the study's conditions they were viewing. The analysis of the coronary lesions before nifedipine was separated from that after the drug by a delay of at least one day in order to avoid that noticeable differences after nifedipine suggested an identity of the circumstance. The interobserver variability was less than 10 percent. The blinding was monitored and the work of the observers coordinated by an assistant.

Statistical Evaluation

Statistical evaluations of the data were performed with the t-test for paired and unpaired analysis when appropriate; correlation of sets of data was sought using a least-squares-fit linear regression analysis; statistical significance was accepted at the level of p<0.05; all grouped data are reported as the mean plus or minus the standard error of the mean (SE).

RESULTS

One hundred and five patients completed the trial. Withdrawals were as follows: three patients refused to cooperate with the placebo and five with the medication during the first phase of active treatment; one patient in group 1 had unstable angina when given placebo and three when given nifedipine; one patient with mixed angina had malignant arrhythmias while receiving placebo and one while receiving active treatment; one patient in group 2 had unstable angina, and one had acute myocardial infarction, both during treatment with nifedipine. No serious complication arose during discontinuation of the previous therapy.

Table 1—Clinical and Angiographic Data from 105 Patients

<table>
<thead>
<tr>
<th>Form of Angina and Coronary arterial Disease</th>
<th>No. of Patients</th>
<th>Age, yr</th>
<th>Range</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>M</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(classic effort-induced)</td>
<td>69</td>
<td>39-65</td>
<td>51 ± 5</td>
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<tr>
<td>Single-vessel</td>
<td>16</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double-vessel</td>
<td>15</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple-vessel</td>
<td>19</td>
<td>6</td>
<td></td>
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</tr>
<tr>
<td>Group 2 (mixed)</td>
<td>22</td>
<td>41-63</td>
<td>53 ± 11</td>
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</tr>
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<td>Single-vessel</td>
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<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double-vessel</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple-vessel</td>
<td>10</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3 (spontaneous)</td>
<td>14</td>
<td>37-51</td>
<td>45 ± 7</td>
<td></td>
</tr>
<tr>
<td>No lesion</td>
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<td>1</td>
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<tr>
<td>Single-vessel</td>
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<td>2</td>
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<td>Double-vessel</td>
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<tr>
<td>Triple-vessel</td>
<td>2</td>
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CHEST / 93 / 3 / MARCH, 1988 487

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Improved changes induced by nifedipine (10 mg sublingually) on residual lumen of 91, 29, and 19 coronary lesions identified as significant (>50 percent) in effort-induced, mixed, and Prinzmetal's angina, respectively. Solid symbols indicate means (± SE).

Classic Effort-Induced Angina

Angiographic Data. Ninety-one coronary lesions identified as significant were analyzed in this group. The effect of sublingual nifedipine on minimal luminal diameter was evaluated for all of these lesions. The minimal luminal diameter was either unchanged, augmented, or diminished following calcium-channel blockade (Fig. 2), and the magnitude and direction of the changes were not related to the size of the residual lumen. The magnitude and direction of these changes did not correlate with the influences of nifedipine (40-mg regimen) on the ST-segment shifts; in fact, several patients who showed enhancement of ST-segment depression had had dilatation of their stenotic lesions.
in the short-term study.

**Holter Monitoring.** No significant ST-segment shift was recorded in this group of patients during the ordinary daily activity.

**Exercise Testing.** Patients in this group were considered improved, unchanged, or worsened by the 10-mg treatment with nifedipine if the mean ST-segment depression, at the same maximal workload attained while receiving placebo, was reduced, unchanged, or enhanced, respectively. As shown in Figure 3, ST-segment depression was reduced in 42 patients (61 percent of the entire population of group 1), unchanged in 14 patients (20 percent), and enhanced in 13 patients (19 percent). In each of these three subgroups, the number of patients with single-vessel, double-vessel, or triple-vessel disease was comparable. When the dose of nifedipine was doubled, the ST-segment depression tended in some cases to be reduced further and in other cases to become enhanced; however, differences between the two regimens did not reach statistical significance. Average variations from the untreated phase of the rate-pressure product at maximal workload with placebo were small with either regimen and statistically were not significant. The double product was dissociated from the ST-segment shifts (Fig 4); in fact, ST-segment depression was either reduced or augmented by treatment with nifedipine when the double product was raised, lowered, or unchanged.

**Mixed Angina**

**Angiographic Data.** In this group, we analyzed 29 significant coronary lesions, one in each of the 22 patients and two in seven of them. Stenotic diameter within the same subject presenting with multiple-vessel disease varied in the same direction under the influence of nifedipine. The effect of the sublingual

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**Figure 4.** Plot of changes with treatment (nifedipine, 10 mg four times daily) from placebo ST-segment shifts during exercise test against changes from placebo rate-pressure product in 50 patients in group 1. No correlations exist between the two variables. Solid square indicates mean (± SE) of changes.

**Figure 5.** Plot of immediate changes induced by nifedipine (10 mg sublingually) on residual lumen of coronary lesions identified as significant (>50 percent) in 22 patients of mixed-angina group against variations with treatment (nifedipine, 10 mg four times daily) in spontaneous (angina episodes/24 hours, left) and effort-associated (ST-segment shift during exercise testing, right) components of angina. Solid symbols identify patients who had full relief of spontaneous anginal episodes.
drug on minimal luminal diameter is summarized in Figure 2. Stenotic dimensions were enhanced in 17 and reduced in 12 cases by the calcium antagonist, with a wide extent of variation (from +1.3 to −1.6 mm), and the pattern did not bear a relationship to the size of the baseline stenotic lumen. Two patients with nifedipine had a transient occlusion at the site of the stenosis of the left anterior descending coronary artery, with associated angina pectoris. Aortic diastolic pressure averaged 77.8 ± 2.2 mm Hg in the baseline and 71.9 ± 2.5 mm Hg when coronary angiography was repeated after nifedipine.

**Holter Monitoring.** The spontaneous component of this form of angina was evaluated through diary records and ambulatory Holter monitoring. With the 10-mg treatment, variations in the number of spontaneous attacks in 24 hours and their relationship with the vasomotor reaction to short-term nifedipine in each patient are outlined in Figure 5 (left). Spontaneous angina (number of attacks per 24 hours) was reduced in eight patients (36 percent), abolished in four patients (18 percent), exacerbated in nine patients (41 percent), and unvaried in one patient. The link between the vasomotor and the clinical response was impressive; in fact, all of the patients who did worse with treatment had constriction of the stenotic lesions; only two who had a small constriction did better; and all of the subjects who had vasodilatation improved.

**Exercise Testing.** Regarding the effort-associated component, the link between the immediate angiographic and the clinical response to treatment (changes in ST-segment shift during exercise testing) was evident, but somewhat less tight than observed for the spontaneous component (Fig 5, right). In fact, the magnitude of ST-segment displacement while receiving nifedipine was unchanged in six patients, enhanced in two patients who had stenotic dilatation, and reduced in one patient who had stenotic constriction. A correlation between the angiographic and the clinical response was observed in the remaining cases.

We tested the 20-mg regimen only in patients in whom the smaller dosage was effective on either component of angina and observed the same results.

**Spontaneous (Prinzmetal's) Angina**

**Angiographic Data.** Acute calcium channel blockade (Fig 2) invariably augmented the dimension of 19 examined coronary lesions, and the minimal diameter rose from an average of 1.7 ± 0.16 mm to 2.8 ± 0.2 mm (+69 percent). The average of aortic diastolic pressure was 79.5 ± 3.5 mm Hg in the baseline and was lowered to 71.5 ± 5.4 mm Hg by nifedipine.

**Holter Monitoring.** Anginal attacks at rest associated with ST-segment elevation ranged from 2 to 36 in the 24 hours (average, 13.4) in these patients; 22 percent of the ischemic episodes were not associated with pain. The lower dosage of nifedipine abolished the ischemic attacks, both painful and painless, in nine patients, and the double dose was fully effective in the remaining cases.

**Exercise Testing.** None of the patients in this group showed significant ST-segment shifts during exercise, both in the untreated and the treated condition.

The response of the normal coronary vessels to nifedipine is another aspect that differentiates Prinzmetal's angina from the other forms. By taking the average of the luminal diameter by proximal, medial, and distal sites, we obtained the mean diameter of 45 normal major epicardial vessels in group 1, of 14 vessels in group 2, and of 17 vessels in group 3. The same measurements were repeated after calcium channel blockade. Figure 6 shows that in response to calcium-channel blockade, the mean vascular lumen in groups 1 and 2 was either slightly increased or decreased or unchanged. On the contrary, no vessel in group 3 reacted to nifedipine with vasodilatation, and the average changes were significantly (p<0.01) greater than in group 1 and in group 2.

**Discussion**

The unpredictability of spontaneous angina makes an objective evaluation difficult, however, several aspects support the consistency of our findings in
spontaneous angina: evaluation for each patient of the control level of attack frequency during the placebo period, that was compared with the attack frequency observed during nifedipine therapy; short duration of the trial, which reduced the likelihood of coincidence with spontaneous remission, evidence that the clinical response in some cases was dose-related. This study confirms that (1) no pattern of the coronary atherosclerotic process is peculiar to the three forms of angina, and the extent and severity of the disease do not predict the clinical response to calcium channel blockade; (2) patients with Prinzmetal's angina exhibit a significantly more favorable response than those with classic exertional angina; (3) nifedipine fails to relieve exertional angina in a considerable number of cases and is no better in treating mixed angina than in treating purely exertional angina; (4) therapy may be associated with increased frequency of angina; and (5) coronary artery segments of both normal and stenotic vessels show either increase or decrease or no change in diameter in response to the calcium channel blocker. 

Our main goal was to evaluate whether there is a relationship between the short-term coronary vasomotor influences of nifedipine and the clinical response to treatment. All patients in group 3 showed significant short-term widening of critical stenoses, as well as an obvious clinical improvement. In group two, 45 percent (ten) of the subjects responded to nifedipine with dilatation of stenotic lesions, and the majority of the subjects showed improvement of both the effort-associated and the spontaneous component of angina. The fact that in this group, almost all patients who did worse with treatment responded to short-term therapy with nifedipine with narrowing of the coronary stenoses, substantiates the view that a cause-effect link between the vasomotor and the clinical response exists in the mixed form of angina.

In group 1, the pressure-rate product's reaction to the calcium blocker, used as an index of myocardial oxygen consumption during exercise, failed to provide an explanation for the clinical results. These data can be interpreted as showing merely that the rate-pressure product's response to exercise is not reproducible or that those patients in whom the double product increased at ischemia during nifedipine therapy had a dynamic component of the coronary stenoses which contributed to flow resistance. The improved exercise response produced by nifedipine may have been at least in part the result of the drug's dilating influences and thereby increasing myocardial flow; however, a correlation was not found between short-term coronary vasomotor reaction and ST-segment response to exercise, suggesting that the short-term vasomotor pattern is an unreliable predictor of the clinical results in effort-induced angina. It seems likely, therefore, that the influence of nifedipine on this form of angina may vary from subject to subject as a result of the interaction and the relative preponderance of changes in myocardial oxygen consumption and supply, the direction and the magnitude of which are unpredictable.

Short-term nifedipine widened or narrowed the stenotic lumen in a considerable number of patients in groups 1 and 2. These effects are not immediately understood. Relaxation of smooth muscle in the compliant portions of the stenosis, which has already been suggested to explain a similar action of nitroglycerin, offers an explanation for the increases in minimal luminal diameter with nifedipine. Narrowing, which in two patients in group 2 was such as to cause obliteration of the stenotic lumen, might take its origin from a reduction of the intraluminal distending pressure or from passive collapse in compliant lesions, due to the drop in pressure through the stenoses consequent on a nifedipine-induced coronary hyperemia. While the perfusion pressure (aortic diastolic pressure) was reduced to a similar extent in groups 2 and 3, the stenotic lumina were narrowed in some of the patients in group 2 and in none of those in group 3. This suggests that reduction of perfusion pressure was not primarily responsible for the stenotic vasoconstriction. Although our data leave the mechanism of narrowing unexplained, it is noteworthy that exacerbation of the coronary stenoses involved 45 percent of the cases in group 2 and that in the same group, the spontaneous and the effort-associated components worsened with nifedipine in 40 and 50 percent of the patients, respectively. Angina with the two components, therefore, appears largely dependent on coronary vasomotion, which may be influenced either favorably or unfavorably by nifedipine; however, we believe that a larger number of observations is needed before the angiographic response may be used to predict the clinical response and assist in the choice of therapy.

The vasomotor activity of calcium channel blockade in Prinzmetal's angina seems peculiar with regard to both stenotic segments and normal coronary vessels. Most stenotic lesions have compliant portions and respond with dilatation, which is significantly greater than in effort-induced and mixed angina. No case showing constriction with nifedipine has been documented in this study. The pathophysiologic significance of this finding is substantiated by an obviously enhanced vasodilating response of the normal epicardial vessels, as compared with both classic and mixed angina. This leads one to speculate that the entire coronary artery wall is hypersensitive to calcium channel blockade, reinforcing the concept that Prinzmetal's angina is a separate disease.
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