Effect of Prazosin vs Placebo on Chronic Left Ventricular Heart Failure

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SUMMARY The effect of the vasodilator prazosin vs placebo on exercise duration until marked dyspnea, and on left ventricular function measured by echocardiography, was evaluated in a double-blind, randomized study in 24 patients with chronic left ventricular failure despite digitalis and diuretic therapy. Compared with the double-blind placebo, prazosin reduced resting systolic and diastolic blood pressure and systolic blood pressure time heart rate, improved clinical symptoms, decreased cardiothoracic ratio measured by chest roentgenography, decreased left ventricular and left atrial dimensions, improved ejection fraction and Vcf measured by echocardiography, and improved treadmill exercise duration. All 12 patients taking prazosin had ≥20% improved treadmill exercise duration; none of 12 receiving placebo improved. In six of 12 patients taking prazosin, roentgenographic evidence of pulmonary venous congestion disappeared compared with none of the patients on placebo. These data suggest that prazosin may be effective in treating chronic left ventricular failure.

ORAL, SUBLINGUAL AND TOPICAL vasodilators are important in the management of severe heart failure.1-17 By reducing ventricular preload, nitrates relieve pulmonary congestion.1-8 By reducing ventricular afterload, oral hydralazine improves cardiac output.5, 8-12 A combination of nitrates and hydralazine may relieve dyspnea by reducing pulmonary congestion and decrease fatigue by increasing cardiac output.5, 8 However, chronic hydralazine therapy may be associated with induction of the systemic lupus erythematosus syndrome.

Oral prazosin has balanced vasodilator effects on the systemic arterial and venous beds.15-16 Preliminary data also show that prazosin improves exercise duration and echocardiographic measurements of ventricular function.15

We performed a double-blind, randomized study to evaluate the effect of prazosin vs placebo on treadmill exercise performance and on ventricular function, measured by echocardiography, in 24 patients with chronic left-sided congestive heart failure unresponsive to digitalis and diuretic therapy.

Methods

The subjects were 24 men 26–67 years of age with chronic left-sided congestive heart failure. Fifteen had documented coronary heart disease. Cardiac catheterization demonstrated significant multivessel coronary artery disease and poor left ventricular function in these subjects. Thirteen of the 15 patients with coronary disease had a documented previous transmural myocardial infarction; two had rheumatic heart disease with severe mitral insufficiency and poor left ventricular function demonstrated by cardiac catheterization; four had idiopathic congestive cardiomyopathy with normal coronary angiograms and diffusely impaired left ventricular contractility; three had alcoholic congestive cardiomyopathy with normal coronary angiograms and diffusely impaired left ventricular contractility.

All 24 patients had cardiomegaly on physical examination and roentgenography, a left ventricular third heart sound on auscultation, and evidence of pulmonary venous congestion. Baseline standing blood pressures ranged from 110–152 mm Hg systolic and from 70–100 mm Hg diastolic. The patients had taken digitalis and diuretic therapy for 2–52 months. Of the 12 patients randomized to prazosin, 11 took furosemide 40–240 mg daily, and one took hydrochlorothiazide 100 mg daily. Of the 12 patients randomized to double-blind placebo, 11 took furosemide 40–160 mg daily and one took hydrochlorothiazide 100 mg daily. Their doses of these drugs were not changed during the study. Except for potassium chloride, no other medications were taken by any patient during this study. All patients signed informed research consent forms.

After baseline measurements, all 24 patients took one capsule of single-blind placebo three times daily for 2 weeks. Then, in a double-blind, randomized fashion, all patients took prazosin or placebo for 6 more weeks. The prazosin and placebo capsules looked identical. Twelve patients took one placebo capsule three times daily for weeks 1 and 2, two placebo capsules three times daily for weeks 3 and 4, and three placebo capsules three times daily for weeks 5 and 6 of the double-blind study period. Twelve patients received one 0.5 mg prazosin capsule three times daily for week 1, one 1 mg prazosin capsule three times daily for week 2, two 1 mg prazosin capsules three times daily for weeks 3 and 4, and three 1

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mg prazosin capsules three times daily for weeks 5 and 6 of the double-blind study.

Each patient answered a standard questionnaire regarding symptoms, had a physical examination in the baseline period, at the end of 2 weeks of the single-blind placebo regimen, and at the end of weeks 1, 2, 3, 4, 5 and 6 in the double-blind study period. A standard 12-lead ECG and posteroanterior and lateral chest roentgenograms were taken in the baseline period, at the end of 2 weeks of the single-blind placebo period, and at the end of 3 weeks and 6 weeks of the double-blind study period.

Echocardiograms were performed in all patients in the baseline period and approximately 105 minutes after their morning dose of medication after 2 weeks of single-blind placebo and after 3 and 6 weeks of double-blind medication. Echocardiography was performed in all patients with an Ekoline-20 ultrasonoscope with a 0.5 inch diameter 2.25 MHz transducer focused at 10 cm with a repetition rate of 1,000 impulses/sec, and an Irex ContinuTrace 101 multichannel recorder. All echocardiograms were recorded with the subjects in a slight left lateral decubitus position with 15° elevation of the head. ECGs were recorded simultaneously with the echocardiograms. The heart rates were measured from the ECGs.

We selected a transducer position from which we could consistently and readily obtain distinct left ventricular dimensions. We determined the transducer position which gave the optimal mitral valve echogram. The transducer was then angled slightly laterally and inferiorly to obtain clear left ventricular septal and posterior wall endocardial echoes. In this position, the mitral valve echogram was discontinuous and the posterior leaflet was usually better visualized. Using the echoes from the mitral valve apparatus as landmarks, we obtained reproducible left ventricular dimensions.18-21 Recordings were made at the constant respiratory phase of held mid-expiration. The left ventricular diameter at end-systole (LVESD) was measured at the point of least separation of the septal and posterior wall endocardial echoes. The left ventricular diameter at end-diastole (LVEDD) was measured at the peak of the R wave in the ECG.

After recognition of the characteristic mitral valve echoes, the transducer was angled medially, posteriorly, and superiorly to record the aortic root and left atrium. Measurements of left atrial dimension were made at ventricular end-systole between the external surface of the posterior aortic root and the internal surface of the left atrial wall.

The ejection time (ET) was calculated as the time from the beginning of the QRS complex to maximal anterior systolic motion of the left ventricular posterior wall minus 50 msec for the preejection period.15, 22 The left ventricular volume at end-systole (LVESV) and at end-diastole (LVEDV) were calculated by the cube of their respective diameters.19 Stroke volume (SV), cardiac index (CI), ejection fraction (EF), and mean rate of left ventricular circumferential fiber shortening (Vcf) were derived as follows:

\[
SV = LVEDV - LVESD
\]

\[
CI = \frac{\text{heart rate} \times SV}{1,000 \times \text{body surface area}}
\]

\[
EF = \frac{SV}{LVEDV}
\]

\[
Vcf = \frac{LVEDD - LVESD}{ET \times LVEDD}
\]

All patients performed two practice treadmill tests within 1 week before the baseline period. After echocardiographic estimation of ventricular function, the patients performed a multistage, uninterrupted maximal treadmill exercise test until the onset of marked dyspnea in the baseline period, approximately 2 hours after their morning dose of medication after 2 weeks of the single-blind placebo study and after 3 and 6 weeks of the double-blind medication study. Marked dyspnea was the limiting factor in all maximal treadmill exercise tests in all patients. The patients exercised at a treadmill speed of 1.7 mph and a treadmill grade of 0% for the first 3 minutes, a treadmill speed of 1.7 mph and a treadmill grade of 10% for the next 3 minutes, and then at a treadmill speed of 2.5 mph and a treadmill grade of 12%.

The patients were monitored with telemetry with simultaneous leads II and V6 throughout exercise. Simultaneous leads II and V6 and blood pressures were recorded with the patients sitting and standing immediately before exercise, with the patients standing at the end of each completed stage of exercise and at the end of exercise, and with the patients in both sitting and standing positions every minute for at least 5 minutes after exercise. Blood pressures were recorded with a mercury sphygmomanometer. The heart rates were measured from the electrocardiographic recordings. Blood pressures were obtained by the same technician. The cardiology fellows supervising the exercise tests did not know the blood pressure readings to maintain a double-blind exercise test. The chest roentgenograms and ECGs were blindly coded and interpreted at the end of the study.

The data listed in tables 1–4 were analyzed using Tukey range tests. Fisher’s exact test was used to analyze the data on improvement of symptoms and the data on changes in roentgenographic evidence of pulmonary venous congestion.

Results

Pill counts revealed that all 24 patients had taken their medication as prescribed. No adverse reactions to medication occurred during the study.

Table 1 shows the hemodynamic values, exercise duration, ST-segment depression and mean cardiothoracic ratio ± SD during the baseline period, after 2 weeks of single-blind placebo, and after 3 and 6 weeks of double-blind placebo. It also shows the causes of the congestive heart failure in the patients randomized to double-blind placebo.

Table 2 indicates the same data for the baseline
Table 1. Hemodynamic Values, Exercise Duration, ST-Segment Depression and Cardiothoracic Ratio During Baseline, Single-Blind Placebo and Double-Blind Placebo Periods (Mean ± 1 sd)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (seconds)</th>
<th>Single-blind placebo</th>
<th>Double-blind placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting heart rate (beats/min)</td>
<td>83.8 ± 9.9</td>
<td>85.1 ± 7.6</td>
<td>84.1 ± 10.4</td>
</tr>
<tr>
<td>Resting systolic blood pressure (mm Hg)</td>
<td>124.2 ± 11.8</td>
<td>125.7 ± 9.2</td>
<td>127.3 ± 10.1</td>
</tr>
<tr>
<td>Resting diastolic blood pressure (mm Hg)</td>
<td>82.3 ± 8.4</td>
<td>82.4 ± 6.5</td>
<td>84.2 ± 7.4</td>
</tr>
<tr>
<td>Exercise heart rate (beats/min)</td>
<td>133.1 ± 14.0</td>
<td>133.6 ± 14.5</td>
<td>133.5 ± 13.2</td>
</tr>
<tr>
<td>Exercise systolic blood pressure (mm Hg)</td>
<td>145.7 ± 12.5</td>
<td>149.2 ± 13.2</td>
<td>149.8 ± 13.4</td>
</tr>
<tr>
<td>Exercise diastolic blood pressure (mm Hg)</td>
<td>90.0 ± 6.6</td>
<td>90.4 ± 5.9</td>
<td>90.5 ± 7.0</td>
</tr>
<tr>
<td>Exercise systolic pressure times heart rate/100</td>
<td>197.4 ± 22.6</td>
<td>198.8 ± 22.8</td>
<td>199.5 ± 20.8</td>
</tr>
<tr>
<td>Exercise duration (sec)</td>
<td>211.9 ± 56.0</td>
<td>221.2 ± 59.7</td>
<td>218.7 ± 54.5</td>
</tr>
<tr>
<td>Maximal ST depression below resting level (mm)</td>
<td>1.42 ± 0.47</td>
<td>1.48 ± 0.45</td>
<td>1.50 ± 0.44</td>
</tr>
<tr>
<td>Cardiothoracic ratio</td>
<td>0.58 ± 0.04</td>
<td>0.58 ± 0.04</td>
<td>0.58 ± 0.04</td>
</tr>
</tbody>
</table>

Eight patients had coronary heart disease; two had congestive cardiomyopathy; two had rheumatic heart disease with severe mitral insufficiency and poor left ventricular function.

Figure 2 shows the percent change in exercise duration for each patient after 6 weeks of double-blind placebo therapy from the average of the baseline and single-blind placebo periods. None of the 12 patients randomized to double-blind placebo had ≥20% improvement in exercise duration.

Table 2 lists the echocardiographic data during the baseline period, after 2 weeks of single-blind placebo, and after 3 and 6 weeks of double-blind placebo. Table 4 indicates the same data for the baseline period, after 2 weeks of single-blind placebo, after 3 weeks of

Table 2. Hemodynamic Values, Exercise Duration, ST-Segment Depression and Cardiothoracic Ratio During Baseline, Single-Blind Placebo and Prazosin Periods (Mean ± 1 sd)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (seconds)</th>
<th>Single-blind placebo (seconds)</th>
<th>Double-blind prazosin (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting heart rate (beats/min)</td>
<td>90.3 ± 11.2</td>
<td>89.6 ± 9.5</td>
<td>86.7 ± 8.2</td>
</tr>
<tr>
<td>Resting systolic blood pressure (mm Hg)</td>
<td>122.8 ± 8.8</td>
<td>124.7 ± 9.2</td>
<td>113.3 ± 7.9*</td>
</tr>
<tr>
<td>Resting diastolic blood pressure (mm Hg)</td>
<td>83.0 ± 7.5</td>
<td>83.0 ± 6.5</td>
<td>75.6 ± 6.1*</td>
</tr>
<tr>
<td>Exercise heart rate (beats/min)</td>
<td>110.8 ± 14.3</td>
<td>111.6 ± 13.7</td>
<td>98.2 ± 11.1†</td>
</tr>
<tr>
<td>Exercise systolic blood pressure (mm Hg)</td>
<td>129.2 ± 10.2</td>
<td>131.3 ± 9.7</td>
<td>131.1 ± 9.1</td>
</tr>
<tr>
<td>Exercise diastolic blood pressure (mm Hg)</td>
<td>148.7 ± 11.2</td>
<td>149.8 ± 13.2</td>
<td>147.7 ± 11.6</td>
</tr>
<tr>
<td>Exercise systolic pressure times heart rate/100</td>
<td>192.4 ± 24.6</td>
<td>197.2 ± 26.6</td>
<td>193.9 ± 23.6</td>
</tr>
<tr>
<td>Exercise duration (sec)</td>
<td>213.3 ± 54.9</td>
<td>225.4 ± 59.0</td>
<td>291.7 ± 71.8†</td>
</tr>
<tr>
<td>Maximal ST depression below resting level (mm)</td>
<td>1.42 ± 0.25</td>
<td>1.37 ± 0.25</td>
<td>1.24 ± 0.26</td>
</tr>
<tr>
<td>Cardiothoracic ratio</td>
<td>0.58 ± 0.04</td>
<td>0.58 ± 0.04</td>
<td>0.57 ± 0.04†</td>
</tr>
</tbody>
</table>

*p <0.001 for prazosin at 3 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 3 weeks minus an average of its baseline and single-blind placebo periods.

†p <0.005 for prazosin at 3 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 3 weeks minus an average of its baseline and single-blind placebo periods.

‡p <0.01 for prazosin at 3 weeks minus an average of its baseline and single-blind placebo periods.

Seven patients had coronary heart disease; five had congestive cardiomyopathy.
Prazosin (6 mg daily), and after 6 weeks of prazosin (9 mg daily). Table 4 also lists statistical levels of significance.

All 12 patients randomized to prazosin had good or excellent relief of symptoms; none of the 12 patients randomized to placebo achieved these results ($p < 0.001$). Six of 12 patients randomized to prazosin had roentgenographic evidence of disappearance of pulmonary venous congestion, while none of 12 patients randomized to placebo had these results ($p = 0.007$).

**Table 3. Echocardiographic Data During Baseline, Single-Blind Placebo and Double-Blind Placebo Periods**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Single-blind placebo</th>
<th>Double-blind placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3 Weeks</td>
<td>6 Weeks</td>
</tr>
<tr>
<td>LVEDD (cm)</td>
<td>5.5 ± 0.9</td>
<td>5.5 ± 0.9</td>
<td>5.5 ± 0.9</td>
</tr>
<tr>
<td>LVESD (cm)</td>
<td>4.5 ± 0.9</td>
<td>4.6 ± 0.9</td>
<td>4.5 ± 0.9</td>
</tr>
<tr>
<td>LAD (cm)</td>
<td>4.4 ± 0.8</td>
<td>4.3 ± 0.7</td>
<td>4.4 ± 0.8</td>
</tr>
<tr>
<td>Systolic ejection time (msec)</td>
<td>237.9 ± 29.2</td>
<td>235.0 ± 29.7</td>
<td>237.5 ± 34.5</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>75.5 ± 31.6</td>
<td>75.8 ± 34.1</td>
<td>73.3 ± 30.3</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>3.28 ± 1.42</td>
<td>3.26 ± 1.49</td>
<td>3.14 ± 1.25</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>44.5 ± 9.4</td>
<td>43.7 ± 9.0</td>
<td>44.2 ± 8.9</td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>0.76 ± 0.19</td>
<td>0.75 ± 0.17</td>
<td>0.75 ± 0.16</td>
</tr>
</tbody>
</table>

Abbreviations: LVEDD = left ventricular dimension at end-diastole; LVESD = left ventricular dimension at end-systole; LAD = left atrial dimension; Vcf = mean rate of left ventricular circumferential fiber shortening.

Figure 3 is the chest roentgenogram during the baseline period in a patient randomized to prazosin therapy, and figure 4 is the chest roentgenogram in the same patient after 6 weeks of prazosin therapy.

Baseline characteristics between the patients randomized to prazosin and to double-blind placebo showed inequalities in four of the 19 parameters listed in tables 1 and 2 — EF, ($p < 0.01$), LVEDD ($p < 0.01$), LVESD ($p < 0.01$), and Vcf ($p < 0.01$). However, the inequalities in these four baseline characteristics did not influence the therapeutic response to prazosin.

**Discussion**

Prazosin has been shown to cause a prolonged dilating action on both the arterial and venous systems. As a result, it relieves congestive heart failure by reducing left ventricular filling pressure and by reducing impedance with augmentation of cardiac output. The studies by Miller and associates and Mehta and associates and this study also show that
prazosin does not significantly change heart rate in patients with congestive heart failure.

Our study demonstrated that in patients with chronic left-sided congestive heart failure unresponsive to digitalis and diuretic treatment, prazosin effectively lowered resting systolic and diastolic blood pressure and product of systolic blood pressure times heart rate, improved clinical symptoms, decreased the size of the heart measured by chest roentgenography and echocardiography, improved roentenographic evidence of pulmonary venous congestion, improved ventricular function measured by echocardiography, and improved exercise tolerance until marked dyspnea. Our patients tolerated prazosin without side effects. These data confirm the preliminary data reported by Awan and associates.13 The 56% increase in exercise duration after 6 weeks of prazosin in our study is similar to the 52% improvement in exercise duration resulting from prazosin therapy reported by Awan and associates.15

Patients with ischemic heart disease may have regional wall motion abnormalities which may not be detected by echocardiography. The echocardiographic determination of left ventricular performance and volumes in patients with ischemic heart disease may be misleading. However, despite these limitations, directional changes in indices of left ventricular performance and volumes are probably valid.

The product of systolic blood pressure times heart rate at the end of maximal exercise was similar after prazosin and double-blind placebo, indicating that prazosin probably causes no change in myocardial oxygen supply. However, compared with double-blind placebo, prazosin decreased the product of systolic blood pressure times heart rate at rest and at the greatest common exercise load, and reduced the size of the heart, decreasing the myocardial oxygen demand. Improved ventricular function with reduced

### Table 4. Echocardiographic Data During Baseline, Single-Blind Placebo and Double-Blind Prazosin Periods (Mean ± 1 SD)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Single-blind placebo</th>
<th>Double-blind prazosin</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD (cm)</td>
<td>6.4 ± 0.5</td>
<td>6.5 ± 0.6</td>
<td>6.4 ± 0.6</td>
</tr>
<tr>
<td>LVESD (cm)</td>
<td>5.7 ± 0.5</td>
<td>5.7 ± 0.6</td>
<td>5.5 ± 0.6</td>
</tr>
<tr>
<td>LAD (cm)</td>
<td>4.4 ± 0.6</td>
<td>4.5 ± 0.6</td>
<td>4.3 ± 0.5†</td>
</tr>
<tr>
<td>Systolic ejection time (msec)</td>
<td>230.0 ± 33.2</td>
<td>228.8 ± 25.1</td>
<td>229.2 ± 26.4</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>82.8 ± 23.0</td>
<td>85.3 ± 21.7</td>
<td>88.4 ± 19.3</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>3.79 ± 1.30</td>
<td>3.84 ± 1.26</td>
<td>3.95 ± 1.08</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>30.8 ± 7.0</td>
<td>31.6 ± 4.9</td>
<td>34.4 ± 5.1</td>
</tr>
<tr>
<td>Vef (circ/sec)</td>
<td>0.51 ± 0.12</td>
<td>0.52 ± 0.10</td>
<td>0.58 ± 0.10</td>
</tr>
</tbody>
</table>

*p <0.001 for prazosin at 6 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 6 weeks minus an average of its baseline and single-blind placebo periods.

†p <0.005 for prazosin at 6 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 6 weeks minus an average of its baseline and single-blind placebo periods.

‡p <0.05 for prazosin at 3 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 6 weeks minus an average of its baseline and single-blind placebo periods.

* or ‡ for prazosin at 6 weeks minus an average of its baseline and single-blind placebo periods, compared with double-blind placebo at 6 weeks minus an average of its baseline and single-blind placebo periods.

Abbreviations: LVEDD = left ventricular dimension at end-diastole; LVESD = left ventricular dimension at end-systole; LAD = left atrial dimension; Vef = mean rate of left ventricular circumferential fiber shortening.

**Figure 3.** Posteroanterior chest roentgenogram during baseline period in patient with cardiomegaly and pulmonary venous congestion.
ventricular dimensions and left ventricular wall tension and decreased myocardial oxygen demand relative to myocardial oxygen supply was probably responsible for the increased exercise tolerance after prazosin.

There were baseline inequalities in echocardiographic measurements of EF, LVEDD, LVESD, and Vcf between the prazosin and double-blind placebo groups. The results of the single-blind placebo intervention in both the prazosin and double-blind placebo groups support the conclusion that these baseline inequalities did not influence the therapeutic response to prazosin. However, to correct for these baseline imbalances, we compared prazosin and double-blind placebo within the framework of a one-way analysis of covariance. This analysis showed that these baseline inequalities did not alter our conclusions regarding beneficial effects of prazosin vs double-blind placebo on clinical symptoms, blood pressure, exercise performance, cardiothoracic ratio, pulmonary venous congestion, and left ventricular dimensions and function.

While the combination of hydralazine with long-acting nitrates may relieve pulmonary congestion and increase cardiac output, 5, 8 oral prazosin has the advantage of a single drug accomplishing the same thing. 12, 15, 23 Moreover, prazosin does not have the disadvantage of hydralazine's side effects.

Further data should define the role of vasodilating drugs in the chronic treatment of left ventricular failure. Double-blind hemodynamic and exercise crossover studies must be performed to compare the efficacy and side effects of the vasodilator agents.

Acknowledgment

We thank David S. Salsburg, Ph.D., for biostatistical analysis of the data and Colin R. Taylor, M.B., Pfizer, Inc., for supplying the prazosin and placebo.

References

Deep Venous Thrombosis of the Upper Extremity: A Reappraisal

STEPHEN M. PRESCOTT, M.D. AND GERASIM TIKOFF, M.D.

SUMMARY Deep venous thrombosis (DVT) of the upper extremity is an unusual thrombotic event (1–2% of all DVT) which can be conveniently divided into two categories, traumatic (including “stress”) and spontaneous. The spontaneous form is not reported as often in the literature, but occurs more commonly than the traumatic form. There is an increased left-sided predominance in spontaneous DVT compared with the traumatic form, where a right-sided predominance exists. Possible anatomical and physiological explanations are offered for the left-sided predominance in spontaneous DVT of the upper extremity. The thrombogenesis of DVT of the upper extremity is compared with DVT of the lower extremity. An analysis of responses to therapy and considerations for other therapeutic approaches are offered.

DEEP VENOUS THROMBOSIS (DVT) of the lower extremity is widely recognized as a leading cause of morbidity and mortality in adult patients.1,2 DVT of the upper extremity is much less common, occurring with an incidence estimated at 1–2% of that of DVT of the lower extremity.3,4 We were interested in this disparity and the possibility that study of DVT of the upper extremity might provide some insights into the broader problem of venous thromboembolism. We were struck by significant differences between our series of patients and patients reported previously,5–7 and therefore reviewed our experience with DVT of the upper extremity and the available literature. Our analysis suggests that:

1) There is no agreement regarding the best terminology for the subgroups of this disorder. We use a scheme (table 1) similar to that of Coon and Willis,8 which divides thrombosis into traumatic and spontaneous (nontraumatic). Stress, or effort, thromboses are a subset of the traumatic category,4 as their pathogenesis and clinical importance seem closely similar to those of a thrombosis due to clavicular fracture. In contrast, we feel that other “secondary” forms of thromboses (i.e., congestive heart failure, malignancy) have different characteristics (and perhaps pathogenesis) from those resulting from clavicular fracture or “stress.”

2) The relative incidence of the two groups is different from that frequently suggested by the literature, as selection bias in favor of stress thromboses exists in a number of review articles. Preferential lateralization occurs toward the left side in the spontaneous thromboses in contrast to the usual right-sided predominance in “stress” thromboses. Plausible anatomical and physiological reasons explain this preferential localization.

3) Differences and similarities exist between thrombogenesis in the deep veins of the lower and upper extremities.

4) Prompt administration of anticoagulants is the preferred therapy, and anatomical localization of DVT of the upper extremity may be useful in predicting the late outcome of therapy.

Materials and Methods

We studied 12 patients with 14 clinical episodes of DVT of the upper extremity. Most of them were referred to us by the physicians at hospitals affiliated with the University of Utah, but were otherwise unselected. Bias can be inherent in any referral population, but we feel that our patients are at least as representative of the disorder as patients referred...
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