Epinephrine-Induced Reversal of Verapamil’s Electrophysiologic and Therapeutic Effects in Patients With Paroxysmal Supraventricular Tachycardia

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The purpose of our study was to determine whether an infusion of epinephrine reverses the electrophysiologic effects of verapamil and whether reversal of verapamil’s effects on the induction of paroxysmal supraventricular tachycardia (PSVT) by epinephrine during electropharmacologic testing is predictive of stress-related recurrences of PSVT during long-term treatment with verapamil. The infusion rates of epinephrine used in this study were 25 and 50 ng/kg/min, which previously have been demonstrated to result in plasma epinephrine concentrations in the range that occurs during a variety of stresses in humans. The subjects of this study were 17 patients with recurrent PSVT who underwent an electrophysiologic study in the control state and after at least 2 days of treatment with 240–480 mg/day verapamil. After assessing the response to verapamil, epinephrine was infused and testing was repeated. Verapamil significantly slowed atrioventricular conduction and prolonged refractoriness in the atrium and atrioventricular node. The effects of the two infusion rates of epinephrine were generally similar in magnitude and, therefore, the results were pooled. Epinephrine partially or completely reversed all of verapamil’s electrophysiologic effects. Verapamil suppressed the induction of sustained PSVT in 15 patients. Epinephrine facilitated the induction of PSVT in seven of these 15 patients. All 15 patients were treated on a long-term basis with verapamil. The eight patients in whom epinephrine did not facilitate the induction of PSVT had no recurrences of PSVT during 9–18 months of follow-up. In contrast, there were multiple recurrences of PSVT in six of the seven patients in whom epinephrine had facilitated the induction of PSVT, and in five of these patients the episodes of PSVT occurred exclusively during exertion or emotional stress. These five patients then were treated with verapamil and 50 mg/day atenolol. Three patients could not tolerate this combination; however, the remaining two patients had no further recurrences of PSVT. In conclusion, physiologic doses of epinephrine attenuate the electrophysiologic effects of verapamil and may reverse verapamil’s effects on the induction of PSVT during electropharmacologic testing. Reversal by epinephrine of verapamil’s effects on the induction of PSVT may accurately identify patients who are likely to experience stress-related recurrences of PSVT and who may benefit from treatment with a β-blocker during long-term therapy with verapamil. (Circulation 1989;79:783–790)

A physiologic increase in circulating epinephrine has been demonstrated to shorten atrial and atrioventricular (AV) nodal refractoriness and to accelerate AV nodal conduction.¹ These effects are opposite to those of verapamil, which is used to treat patients with paroxysmal supraventricular tachycardia (PSVT).²,³ Therefore, it is possible that a stress-related rise in circulating epinephrine could reverse the therapeutic effects of verapamil in patients with PSVT. The purpose of our study was to investigate this possibility by determining the electrophysiologic effects of an increase in circulating epinephrine in patients with PSVT treated with verapamil. In addition, patients were followed on a long-term basis to determine whether the response to epinephrine dur-
ing electropharmacologic testing predicts stress-related recurrences of PSVT during long-term therapy with verapamil.

Methods

Characteristics of Subjects

The subjects of this study were 17 patients who had recurrent PSVT, underwent an electrophysiology study, and had inducible sustained PSVT in the baseline state. Patients who previously had failed or not tolerated a clinical trial of verapamil were excluded from this study, as were patients who had the Wolff-Parkinson-White syndrome or overt ventricular preexcitation. In addition, three patients who were entered into the study were excluded after undergoing the baseline electrophysiology study because of intolerance to verapamil.

There were seven men and 10 women and their mean age was 45 ± 17 years (±SD). One patient who had coronary artery disease and a history of myocardial infarction had a left ventricular ejection of 0.26; the other 16 patients had no evidence of structural heart disease and had normal left ventricular ejection fractions as determined by a radioisotope ventriculogram or two-dimensional echocardiogram. The average yearly frequency of episodes of symptomatic PSVT ranged from 6 to approximately 50, with the first episode of tachycardia having occurred 6 months to 13 years (mean, 4.8 ± 4 years) before the electrophysiology study. The mechanism of PSVT as determined during electrophysiologic testing was AV nodal reentry in 11 patients, intra-atrial reentry in three patients, and orthodromic reciprocating tachycardia using a concealed accessory AV connection in three patients. Standard criteria that have been previously published were used to determine the mechanism of PSVT. The criteria used to diagnose AV nodal reentry included 1) a discontinuous AV nodal conduction curve, 2) concentric atrial activation during tachycardia and ventricular pacing, 3) requirement of a critical atrial-His interval during induction of tachycardia by an atrial extrastimulus, and 4) absence of criteria for orthodromic reciprocating tachycardia. The criteria used to diagnose orthodromic reciprocating tachycardia included the ability to preexcite the atria during tachycardia by a ventricular depolarization coincident with the His bundle depolarization, the same pattern of eccentric atrial activation during tachycardia and during ventricular pacing, and an increase in the His-atrial interval during tachycardia in association with a functional bundle branch block. The criteria used to diagnose intra-atrial reentry included 1) induction of tachycardia by an atrial extrastimulus independent of conduction to the His bundle or ventricle, 2) continuation of the tachycardia in the presence of AV block, 3) a variable AV relation during tachycardia, and 4) eccentric atrial activation during tachycardia, but concentric atrial activation or ventriculoatrial (VA) dissociation during ventricular pacing at a cycle length similar to the tachycardia cycle length.

Electrophysiology Study

Electrophysiologic studies were performed in the fasting, unsedated state after informed consent was obtained and at least five half-lives after discontinuation of all antiarrhythmic drugs. The study protocol was approved by the Human Research Committee at the University of Michigan. Quadrupolar electrode catheters were positioned in the right atrium, coronary sinus, right ventricular apex, and across the tricuspid valve to record the His bundle electrogram. Leads V₁, I, and III and the intracardiac electrograms were recorded at a paper speed of 100 mm/sec on a Siemens-Elema Mingograf-7 recorder. Pacing was performed with a programmable stimulator with stimuli 2 msec in duration and twice diastolic threshold.

The variables measured during the electrophysiology study included the spontaneous sinus cycle length, arterial pressure, and AV nodal and infranodal conduction times (AH and HV intervals, respectively) during right atrial pacing at cycle lengths of 600 and 500 msec. The longest pacing cycle lengths associated with AV and VA block were determined by incremental atrial or ventricular pacing in steps of 10 msec. Effective and functional refractory periods of the atrium and AV node were determined with a basic drive cycle length of 600 or 500 msec and an extrastimulus scanned in steps of 10 msec. In six patients, the AV nodal effective refractory period was less than the atrial functional refractory period and, therefore, could not be determined. PSVT was induced by overdrive pacing or programmed atrial or ventricular pacing with one or two extrastimuli, and the cycle length and AH, HV, and VA intervals during tachycardia were measured. The VA interval during tachycardia was not measured in the three patients who had an atrial tachycardia.

Sustained PSVT was defined as PSVT more than 30 seconds in duration and nonsustained PSVT was defined as PSVT terminating spontaneously in 30 seconds or less.

Infusion of Epinephrine

Epinephrine infusion rates of 25 and 50 ng/kg/min were used in this study. The plasma epinephrine concentrations resulting from these infusion rates have been measured previously in a group of 40 patients under circumstances similar to those in the present study and were found to fall within the range of plasma epinephrine concentrations that occurs during a wide variety of stresses in humans. Ten minutes of infusion are required to attain a steady-state plasma epinephrine concentration, and, therefore, to ensure that steady-state conditions had been achieved, epinephrine was infused for 14 minutes before its electrophysiologic effects
were measured. There were no adverse reactions to the infusion of epinephrine.

**Study Protocol**

In eight patients, the effects of 25 ng/kg/min epinephrine were determined at the time of the baseline electrophysiologic study in the absence of verapamil. To avoid patient discomfort, the effects of the 50 ng/kg/min infusion of epinephrine were not determined in the control state.

On completion of the baseline electrophysiologic study, all patients were treated with verapamil at a daily dose of 240–480 mg. After at least 2 days of therapy with verapamil, a second electrophysiologic study was performed. The electrophysiologic study was timed to coincide with the last 60–90 minutes of the verapamil dosing interval. After measurement of verapamil’s effects, epinephrine was infused at a rate of 25 ng/kg/min in eight patients and 50 ng/kg/min in nine patients. The effects of epinephrine were determined after 14 minutes of infusion. Attempts to induce PSVT after treatment with verapamil and verapamil plus epinephrine included overdrive pacing and programmed atrial and ventricular stimulation with one and two extrastimuli, as in the control study.

The plasma verapamil concentration was measured after verapamil’s effects were determined (just before initiation of the epinephrine infusion) and again after epinephrine’s effects were determined. The time interval between the two determinations of the verapamil plasma concentration ranged from 25 to 30 minutes.

**Long-Term Treatment With Verapamil**

Among the patients in whom verapamil was effective in suppressing the induction of PSVT during electropharmacologic testing, treatment with verapamil was continued after discharge from the hospital, regardless of the response to the infusion of epinephrine. All patients were followed on a regular basis by one of the authors or the patient’s personal physician. Each patient was interviewed by one of the authors either in person or by telephone and quizzed regarding symptomatic recurrences of PSVT and the circumstances under which these recurrences occurred. Treatment with a β-adrenergic blocking agent (atenolol) was initiated in combination with verapamil in the subjects who had recurrent symptoms of PSVT while being treated with verapamil alone.

**Analysis of Data**

The effects of epinephrine in the absence of verapamil were analyzed with a paired t test. The effects of verapamil and verapamil plus epinephrine on each variable were analyzed with a repeated measures analysis of variance. The effects of the two infusion rates of epinephrine also were compared with a repeated measures analysis of variance. Multiple comparisons were performed with Fisher’s least significant difference procedure. A mixed model analysis of variance was used to analyze the data for the variables that had missing data. A p value of less than 0.05 was considered significant.

**Results**

**Effects of Epinephrine in the Absence of Verapamil**

The effects of 25 ng/kg/min epinephrine were determined in eight patients in the absence of verapamil. The mean dose of epinephrine in these patients was 1.8 ± 3 μg/min. The effects of epinephrine are described in Table 1. Epinephrine significantly decreased the sinus cycle length, AH interval, longest pacing cycle length associated with 1:1 AV and VA block, and the refractory periods of the atrium and AV node. In a patient who had a concealed accessory AV connection, epinephrine shortened the retrograde effective refractory period of the accessory AV connection from 240 to 220 msec.

Epinephrine by itself did not provoke PSVT in any patient. Epinephrine shortened the mean cycle length of induced tachycardia from 345 ± 44 to 321 ± 44 msec (p < 0.01). The mean AH interval during PSVT decreased significantly in response to epinephrine, but there was no change in the mean HV or VA intervals during tachycardia (Table 1).

**Electrophysiologic Effects of Verapamil and Verapamil Plus Epinephrine**

Verapamil resulted in a significant increase in the sinus cycle length, AH interval, longest pacing
Table 2. Effects of Verapamil and Verapamil Plus Epinephrine in 17 Subjects

<table>
<thead>
<tr>
<th></th>
<th>B (msec)</th>
<th>V (msec)</th>
<th>V and E (msec)</th>
<th>V vs. B</th>
<th>V and E vs. V</th>
<th>V and E vs. B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus CL</td>
<td>716±109</td>
<td>807±126</td>
<td>680±100</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>95±10</td>
<td>88±13</td>
<td>86±10</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial ERP (msec)</td>
<td>194±28</td>
<td>227±22</td>
<td>209±29</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Atrial FRP (msec)</td>
<td>234±30</td>
<td>280±29</td>
<td>254±29</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AH interval (msec)*</td>
<td>98±35</td>
<td>163±64</td>
<td>99±25</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>HV interval (msec)*</td>
<td>47±9</td>
<td>47±8</td>
<td>46±7</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>AV block CL (msec)†</td>
<td>326±51</td>
<td>458±100</td>
<td>380±64</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VA block CL (msec)†</td>
<td>302±68</td>
<td>473±152</td>
<td>396±102</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AV node ERP (msec)</td>
<td>253±28</td>
<td>363±61</td>
<td>278±21</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td>AV node FRP (msec)</td>
<td>399±55</td>
<td>460±57</td>
<td>410±48</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
</tbody>
</table>

All values are mean±SD.
B, baseline; E, epinephrine; V, verapamil; AV, atrioventricular; CL, cycle length; ERP, effective refractory period; FRP, functional refractory period; MAP, mean arterial pressure; NS, not significant; VA, ventriculoatrial.
*Measured at the same atrial pacing cycle length (500 or 600 msec).
†Longest atrial or ventricular pacing cycle length associated with block.

The mean doses of epinephrine in the eight patients who received the 25 ng/kg/min infusion of epinephrine and in the nine patients who received the 50 ng/kg/min infusion of epinephrine were 1.8±0.3 and 3.7±0.5 μg/min, respectively. The effect of the 50 ng/kg/min infusion of epinephrine on the AV nodal refractory periods was greater in magnitude than the effect of the 25 ng/kg/min infusion. However, for each of the other variables, the effects of the two infusion rates did not differ significantly, and therefore the results are presented in combined fashion (Table 2). Epinephrine partially reversed verapamil's effects on the atrial refractory periods and on the longest pacing cycle lengths associated with AV and VA block. The effects of verapamil on the AH interval and on the AV nodal refractory periods were completely reversed by epinephrine.

**Comparison of Epinephrine's Electrophysiologic Effects in the Absence and Presence of Verapamil**

The effects of 25 ng/kg/min epinephrine in the absence and presence of verapamil were compared in eight subjects in whom epinephrine was infused both in the baseline state and after treatment with verapamil. The effect of epinephrine on the AH interval in absolute terms was greater in magnitude in the presence of verapamil than in the absence of verapamil (p<0.05). For each of the other electrophysiologic variables, there was no significant difference between the magnitude of epinephrine's effects in the absence and presence of verapamil.

**Effects of Verapamil and Verapamil Plus Epinephrine on Induced PSVT**

The effects of verapamil and epinephrine on induced PSVT are described in Table 3. In accord with the criteria used to select subjects for this study, sustained PSVT was inducible in the baseline state in every patient. Verapamil completely suppressed the induction of PSVT in 13 of 17 patients. In two patients, only nonsustained PSVT was inducible after treatment with verapamil, with the maximum duration of PSVT being four beats on multiple induction attempts. In the remaining two patients, sustained PSVT was still inducible despite treatment with verapamil.

Among the 13 patients in whom verapamil completely suppressed the induction of PSVT, epinephrine facilitated the induction of sustained PSVT in four patients and nonsustained PSVT up to 15 seconds in duration in one patient. Among the two patients in whom a maximum of four beats of PSVT was inducible after treatment with verapamil, either sustained PSVT or nonsustained PSVT 20 seconds in duration became inducible after the infusion of epinephrine. Among the two patients in whom sustained PSVT was inducible after treatment with verapamil, sustained PSVT again was inducible after the infusion of epinephrine, with a 50–60 msec decrease in tachycardia cycle length.

**Verapamil Plasma Concentrations**

The mean plasma verapamil concentrations before and after determination of epinephrine's effects were 203±67 and 202±62 μg/l, respectively (p>0.05). Among the 15 patients in whom verapamil suppressed the induction of sustained PSVT, the mean plasma verapamil concentration after infusion of epinephrine did not differ significantly between the seven patients in whom epinephrine reversed the effects of verapamil on the induction of PSVT and the eight patients in whom it did not (208±58 compared with 196±76 μg/l, respectively; p>0.05).

**Clinical Response to Verapamil**

The 15 patients in whom PSVT was either non-inducible or only up to four beats in duration during
electropharmacologic testing with verapamil were treated on a long-term basis with verapamil. The clinical response to verapamil is described in Table 4.

There were no recurrences of symptomatic PSVT among the eight patients in whom epinephrine had not reversed the effects of verapamil during electropharmacologic testing. The mean duration of follow-up in these patients was 14±4 months (range, 9–18 months).

In contrast, among the seven patients in whom epinephrine reversed the effects of verapamil on the induction of PSVT, six had multiple recurrences of symptomatic PSVT starting within the first 3 months of therapy with verapamil. The episodes of PSVT occurred exclusively in the setting of exertion or emotional stress in five of these patients and on an apparently random basis in one patient.

**Management of Patients With Recurrent PSVT**

Among the six patients who experienced recurrent PSVT despite treatment with verapamil, one patient (12) elected to undergo surgical division of a concealed accessory AV connection; this patient had no further symptoms of PSVT. Five patients underwent a trial of 50 mg/day atenolol in combination with verapamil. Two of these patients (13 and 15) had no further recurrences of symptomatic PSVT during 8–14 months of follow-up. However, the other three patients could not tolerate the combination of verapamil and atenolol because of symptomatic bradycardia or hypotension or both. The latter three patients have been treated with encainide, quinidine plus verapamil, or verapamil alone, and they continue to have occasional episodes of symptomatic PSVT during physical activity or emotional stress.

**Discussion**

Previous studies have determined the plasma epinephrine concentrations that result from the same infusion rates of epinephrine used in the present study.1,9 A 25 ng/kg/min infusion of epinephrine raises the arterial plasma epinephrine concentration to a mean of 862±226 pg/ml;

A 50 ng/kg/min infusion raises the plasma epinephrine concentration to a mean of 1,374±477 pg/ml; this level is within the range that occurs during maximal exercise,9 myocardial infarction,14,15 diabetic ketoacidosis,10 and severe hypoglycemia.10 Therefore, the epinephrine infusion rates used in this study resulted in an increase in circulating epinephrine to levels that occur endogenously during a variety of physiologic and pathophysiologic stresses.

The results of this study demonstrate that an increase in circulating epinephrine to levels that occur endogenously during stress significantly attenuates the electrophysiologic effects of verapamil and may reverse the suppression of inducible PSVT that may occur in response to verapamil. Furthermore, the response to epinephrine during electropharmacologic testing correlates with the clinical

**Table 3. Effects of Verapamil and Verapamil Plus Epinephrine on Induced Paroxysmal Supraventricular Tachycardia in 17 Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Type</th>
<th>CL (msec)</th>
<th>Verapamil</th>
<th>Verapamil and epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AVNR</td>
<td>340</td>
<td>NI†</td>
<td>236</td>
</tr>
<tr>
<td>2</td>
<td>IAR</td>
<td>400</td>
<td>NI</td>
<td>294</td>
</tr>
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<td>3</td>
<td>IAR</td>
<td>320</td>
<td>NI</td>
<td>148</td>
</tr>
<tr>
<td>4</td>
<td>AVNR</td>
<td>270</td>
<td>NI‡</td>
<td>295</td>
</tr>
<tr>
<td>5</td>
<td>AVNR</td>
<td>340</td>
<td>NI†</td>
<td>210</td>
</tr>
<tr>
<td>6</td>
<td>AVNR</td>
<td>300</td>
<td>NI†</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>AVNR</td>
<td>430</td>
<td>NI‡</td>
<td>166</td>
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<tr>
<td>8</td>
<td>AVNR</td>
<td>370</td>
<td>NI‡</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>Ortho</td>
<td>320</td>
<td>NI†</td>
<td>271</td>
</tr>
<tr>
<td>10</td>
<td>Ortho</td>
<td>280</td>
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<td>179</td>
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<tr>
<td>11</td>
<td>AVNR</td>
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<td>307</td>
</tr>
<tr>
<td>12</td>
<td>Ortho</td>
<td>350</td>
<td>NI†</td>
<td>237</td>
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<tr>
<td>13</td>
<td>AVNR</td>
<td>280</td>
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<td>14</td>
<td>AVNR</td>
<td>320</td>
<td>4 beats‡</td>
<td>360</td>
</tr>
<tr>
<td>15</td>
<td>IAR</td>
<td>360</td>
<td>4 beats</td>
<td>400</td>
</tr>
<tr>
<td>16</td>
<td>AVNR</td>
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<td>470</td>
</tr>
<tr>
<td>17</td>
<td>AVNR</td>
<td>290</td>
<td>S</td>
<td>340</td>
</tr>
</tbody>
</table>

AVNR, atrioventricular node reentry; IAR, intra-atrial reentry; NI, not inducible; Ortho, orthodromic reciprocating tachycardia; [V], verapamil plasma concentration.

*The tachycardia was sustained in each patient in the baseline state.
†Block in anterograde slow pathway after one or two echo beats.
‡Block in retrograde fast pathway.
response to verapamil, with reversal by epinephrine of verapamil’s effects on the induction of PSVT being predictive of stress-related recurrences of PSVT during long-term treatment with verapamil.

Effects of Epinephrine in the Absence of Verapamil

In the absence of verapamil, epinephrine accelerated anterograde and retrograde AV node conduction, accelerated retrograde conduction through a concealed accessory AV connection, and shortened refractoriness in the atrium and AV node. These effects have been demonstrated to result from stimulation of β-adrenergic receptors by epinephrine.¹

As has been demonstrated previously in response to isoproterenol,¹⁶,¹⁷ epinephrine resulted in a significant shortening of the PSVT cycle length. Analysis of conduction intervals during tachycardia in patients with either AV nodal reentrant or orthodromic reciprocating tachycardia indicated that the effect of epinephrine on the tachycardia cycle length was primarily a result of epinephrine’s positive dromotrophic effect on the anterograde limb of the reentry circuit.

Electrophysiologic Effects of Epinephrine in the Presence of Verapamil

Epinephrine partially or completely reversed all of verapamil’s electrophysiologic effects. Furthermore, for all of the variables measured except the AH interval, the effects of 25 ng/kg/min epinephrine in the presence of verapamil were quantitatively similar to the effects of epinephrine in the control state. Therefore, it is possible that epinephrine’s effects in the presence of verapamil were the result only of stimulation of β-adrenergic receptors, as in the control state. However, direct antagonism by epinephrine of verapamil’s effects on the calcium channel or some other type of interaction between epinephrine and verapamil cannot be ruled out.

In this study, in the presence of verapamil, the 50 ng/kg/min infusion of epinephrine had a greater effect than the 25 ng/kg/min infusion of epinephrine only in the case of AV nodal refractory periods. In contrast, in an earlier study performed with a larger number of subjects in the absence of verapamil, epinephrine’s effects were always dose dependent.¹

It is possible that dose-dependent effects of epinephrine may have been more apparent in this study had the sample sizes been larger. Alternatively, it is possible that verapamil attenuated the effects of only the 50 ng/kg/min dosage of epinephrine, resulting in equalization of the effects of the two epinephrine infusion rates. The latter possibility could have been investigated by comparing the effects of the 50 ng/kg/min infusion of epinephrine in the basal state with the effects of this infusion rate in the presence of verapamil. However, in order to avoid patient discomfort, the effects of the 50 ng/kg/min infusion of epinephrine were not determined in the basal state in this study.

Epinephrine’s Effects on the Induction of PSVT in the Presence of Verapamil

Among the patients in this study in whom verapamil suppressed the induction of PSVT during electropharmacologic testing, infusion of epinephrine facilitated the induction of sustained PSVT in almost 50% of patients. Although the plasma verapamil concentration decreased somewhat during the test-

### Table 4. Clinical Response to Verapamil in 15 Patients in Whom Verapamil Suppressed the Induction of PSVT During Electrophysiologic Testing

<table>
<thead>
<tr>
<th>Patient</th>
<th>V dose (mg/day)</th>
<th>Reversal by E*</th>
<th>Follow-up (mos)</th>
<th>Episodes of recurrent PSVT</th>
<th>Comments</th>
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<tr>
<td>1</td>
<td>480</td>
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<td>18</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>480</td>
<td>No</td>
<td>18</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>480</td>
<td>No</td>
<td>18</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
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<td>480</td>
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<td>16</td>
<td>0</td>
<td>—</td>
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<td>5</td>
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<td>14</td>
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<td>—</td>
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<tr>
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<td>0</td>
<td>—</td>
</tr>
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<td>9</td>
<td>480</td>
<td>Yes</td>
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<td>&gt;20</td>
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<td>480</td>
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<td>18</td>
<td>6†</td>
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<td>14</td>
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</tr>
<tr>
<td>13</td>
<td>480</td>
<td>Yes</td>
<td>14</td>
<td>6†</td>
<td>No more PSVT on V and BB</td>
</tr>
<tr>
<td>14</td>
<td>320</td>
<td>Yes</td>
<td>20</td>
<td>2†</td>
<td>V and BB not tolerated</td>
</tr>
<tr>
<td>15</td>
<td>240</td>
<td>Yes</td>
<td>8</td>
<td>3†</td>
<td>No more PSVT on V and BB</td>
</tr>
</tbody>
</table>

BB, β-blocker; E, epinephrine; PSVT, paroxysmal supraventricular tachycardia; V, verapamil.

*Reversal of verapamil effect by epinephrine during electropharmacologic testing.

†Recurrents of PSVT precipitated exclusively by exertion or emotional stress.
Verapamil was effective in suppressing the induction of sustained PSVT in 88% of patients in this study. This response rate is higher than the 43–75% response rate reported in previous studies.\(^3,21\) The daily dose of verapamil used in these prior studies was 320 mg, whereas many of the patients in the present study received a daily dose of 360–480 mg. Therefore, the higher response rate in the present study may be attributable to the use of larger doses of verapamil.

Previous studies have demonstrated that epinephrine may antagonize the therapeutic effects of quinidine in patients who have either ventricular tachycardia\(^23\) or the Wolff-Parkinson-White syndrome.\(^24\) Other studies have demonstrated that isoproterenol may reverse the effects of amiodarone,\(^16,25\) flecainide,\(^26,27\) and encainide\(^28,29\) in patients with supraventricular tachycardias. The results of these studies suggest that reversal of antiarrhythmic drug effects by \(\beta\)-adrenergic stimulation may be a generalized phenomenon that occurs not only with verapamil but with many antiarrhythmic drugs.

**Conclusions**

In conclusion, electropharmacologic testing with verapamil in the absence of sympathetic activation may not be accurate in predicting recurrences of PSVT related to an increase in circulating epinephrine. In patients who no longer have inducible PSVT during electropharmacologic testing with verapamil, the ability to induce PSVT after infusion of a physiologic dose of epinephrine may identify patients prone to have stress-related recurrences of PSVT during chronic therapy with verapamil. Additional studies are required to determine the value of \(\beta\)-adrenergic blockade in preventing recurrent PSVT attributable to epinephrine-induced antiarrhythmic drug inefficacy.

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**References**


KEY WORDS • epinephrine • verapamil • paroxysmal • supraventricular tachycardia
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