Hemodynamic Effects of Octreotide in Patients With Autonomic Neuropathy

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Background. The somatostatin analogue, octreotide, is being used to treat postprandial hypotension in patients with autonomic neuropathy. Although the therapeutic effect of the drug is presumably secondary to a splanchnic vasoconstrictor action, its effect on splanchnic hemodynamics has never been characterized in patients with autonomic neuropathy. Moreover, it is unknown whether octreotide acts on other vascular beds in this group of patients or whether it affects cardiac output. We, therefore, measured splanchnic, forearm, and systemic vascular resistance and cardiac output before and after administering octreotide (0.4 µg/kg s.c.) to patients with idiopathic autonomic neuropathy and diabetic autonomic neuropathy.

Methods and Results. Splanchnic blood flow was determined from the clearance of indocyanine green in seven patients. We observed that octreotide decreased splanchnic blood flow (from 850±77 to 664±48 ml/min, p<0.005), increased mean blood pressure (from 97±6 to 115±3 mm Hg, p<0.005), and increased splanchnic vascular resistance (from 0.118±0.012 to 0.18±0.018 mm Hg/ml/min, p<0.005). Forearm blood flow was measured by plethysmography in 13 patients. Octreotide increased forearm vascular resistance in patients with idiopathic autonomic neuropathy (n=8) from 19.1±1.0 to 27.2±3.8 mm Hg/ml/min/100 ml forearm volume (p<0.01) and from 25.2±3.9 to 41.0±6.8 mm Hg/ml/min/100 ml (p<0.01) in patients with diabetic autonomic neuropathy (n=5). Cardiac output was measured by two-dimensional echocardiography. Octreotide administration increased cardiac output in five of six patients with idiopathic autonomic neuropathy (from 4.4±0.4 to 5.0±0.5 l/min, p<0.02) and five of five patients with diabetic autonomic neuropathy (from 3.8±0.4 to 5.1±0.4 l/min, p<0.02). Systemic vascular resistance increased in patients with idiopathic autonomic neuropathy from 21.2±2 to 24.9±2.6 (p<0.05) but did not change in patients with diabetic autonomic neuropathy.

Conclusions. The pressor effect of octreotide in patients with autonomic neuropathy is associated with increased splanchnic and forearm vascular resistance and with increased cardiac output. (Circulation 1991;84:168–176)

The somatostatin analogue, octreotide, has a pressor effect in patients with autonomic neuropathy and is being used therapeutically for postprandial hypotension and orthostatic hypotension. The pressor effect of octreotide is poorly understood and apparently unique to patients with autonomic neuropathy insofar as the drug has no effect on blood pressure in healthy subjects. A splanchnic vasoconstrictor effect of octreotide has been described, however, in experimental animals and in humans. In previous clinical studies of octreotide’s effect on splanchnic blood flow, the drug has been given intravenously; the subjects have been either normal controls or patients with cirrhosis, and patients have been fasting. The results, therefore, may not apply to autonomic neuropathy patients who are administered the drug subcutaneously generally immediately before or after eating.

The purpose of the present study was to characterize the hemodynamic effects of octreotide in patients with autonomic neuropathy. Octreotide’s effect on the splanchnic circulation was assessed in seven patients by measuring postprandial indocyanine green clearance...
after administration of the drug (0.4 µg/kg octreotide) or a placebo. Forearm vascular resistance was assessed in 13 patients by measuring postprandial forearm blood flow after octreotide (0.4 µg/kg) or placebo. Eleven of the patients participated in a similar but separate protocol in which fasting rather than postprandial forearm blood flow was measured. Octreotide’s effects on splanchnic and forearm blood flow were compared with those of dihydroergotamine, a vasoconstrictor thought to have no effect on the splanchnic vasculature, which generally fails to prevent postprandial hypotension.8 We also assessed the effect of octreotide on systemic hemodynamic responses and cardiac filling and measured cardiac output and systemic vascular resistance before and after octreotide administration.

**Methods**

**Patients**

Thirteen patients with autonomic neuropathy and orthostatic hypotension participated in these studies. Eight had idiopathic autonomic neuropathy secondary to either peripheral autonomic dysfunction (pure autonomic failure, \( n = 5 \)) or central nervous system disease (multiple system atrophy, \( n = 3 \)). Five patients had diabetic autonomic neuropathy. Three of the patients with pure autonomic failure and two of those with diabetic autonomic neuropathy were hypertensive when supine. The orthostatic hypotension was chronic in all patients and could not be attributed to dehydration or adrenal cortical insufficiency. Postprandial hypotension, a decrease in mean blood pressure of at least 15 mm Hg during the first 60 minutes after food ingestion, was present in all the patients with idiopathic autonomic neuropathy but none of the patients with diabetic autonomic neuropathy. The diabetic patients had multiple signs and symptoms of polyneuropathy including foot ulcers, chronic diarrhea, and gastroparesis diabetorum. Six healthy elderly subjects in excellent health volunteered to serve as controls. They were age matched to the patients with idiopathic autonomic neuropathy but older than those with diabetic autonomic neuropathy (Table 1).

Autonomic function was assessed in all participants as previously described.3 All the patients with idiopathic autonomic neuropathy and four of five patients with diabetic autonomic neuropathy had little or no increase in heart rate despite large decreases in blood pressure associated with shifting from the supine to the upright posture (Table 1). Plasma norepinephrine was decreased in the patients with idiopathic autonomic neuropathy when they were either supine or upright for 3–5 minutes. Only one of the patients with diabetic autonomic neuropathy, however, had low plasma norepinephrine concentrations (139 pg/ml supine, 104 pg/ml upright).

Twelve of the patients with autonomic neuropathy were able to perform vasomotor reflex tests; 10 showed little or no bradycardia after the Valsalva maneuver (a Valsalva ratio less than 1.1), and 11 had diminished beat-to-beat variation with deep breathing (less than 10 beats/min). Further confirmation of autonomic neuropathy was derived from analysis of autonomic surface potentials, an index of sympathetic sudomotor function. Autonomic surface potentials were absent in the soles of all the patients with diabetic autonomic neuropathy and multiple system atrophy. Two of the patients with pure autonomic failure had absent responses, and three had normal low-amplitude responses (0.1–0.25 mV).

The patients were told that these studies were experimental, and informed consent was obtained. All protocols were approved by Temple University Hospital Institutional Review Board.

**Experimental Methods**

All studies were performed in patients hospitalized in Temple University General Clinical Research Center. Patients were administered a diet containing 110–130 mmol Na/day. Caffeine-containing beverages and cigarette smoking were not allowed. Fludrocortisone, 0.2 mg/day, was administered to those patients who did not have supine hypertension.

**Table 1. Clinical Characteristics of Patients**

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients and sex</th>
<th>Mean (range) age (yr)</th>
<th>Mean blood pressure (mm Hg) Supine Upright</th>
<th>Plasma norepinephrine (pg/ml) Supine Upright</th>
<th>Valsalva Bradycardia Tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure autonomic failure</td>
<td>3 M 2 F</td>
<td>71 (42–86)</td>
<td>118±9 63±9*</td>
<td>155±23 199±26*</td>
<td>1.08±0.05†</td>
</tr>
<tr>
<td>Multiple system atrophy</td>
<td>2 M 1 F</td>
<td>71 (68–77)</td>
<td>108±2 56±5*</td>
<td>207±44 207±44*</td>
<td>1.01±0.01†</td>
</tr>
<tr>
<td>Diabetic autonomic neuropathy</td>
<td>2 M 3 F</td>
<td>39 (17–62)</td>
<td>104±8 65±3*</td>
<td>209±39 322±64</td>
<td>1.09±0.04†</td>
</tr>
<tr>
<td>Controls</td>
<td>2 M 4 F</td>
<td>68 (59–78)</td>
<td>95±7 99±6</td>
<td>347±19 626±42</td>
<td>1.22±0.04</td>
</tr>
</tbody>
</table>

Data are mean±SEM. Plasma norepinephrine concentrations of the patients with diabetic autonomic neuropathy were not compared with those of controls because these groups were not age matched.

\*p<0.01, †p<0.05, patients with autonomic neuropathy were significantly different from controls.
**Measurement of Splanchnic Blood Flow**

Indocyanine green clearance can be used as an index of splanchnic blood flow because numerous studies have established that the dye is normally confined to the systemic circulation and cleared from the blood stream exclusively by hepatic mechanisms.\(^1\) Seven patients (three with pure autonomic failure, three with multiple system atrophy, and one with diabetic autonomic neuropathy) and four control subjects participated in this protocol. Patients known to be allergic to iodine were excluded from participation. All studies were performed after an overnight fast with patients in a semirecumbent position (head of bed elevated 30\(^\circ\)); two autonomic neuropathy patients with supine hypertension were studied while sitting in a chair. Intravenous catheters were placed in the forearms of both arms, one for administering the indocyanine green and the other for withdrawing blood to determine the serum concentrations of the dye.\(^2\) Because many of the patients were elderly and debilitated and because some developed severe hypotension after eating, hepatic vein catheterization was not performed. We assumed the hepatic extraction of indocyanine green was 0.8.\(^3\)\(^4\)\(^5\)\(^6\)

Arterial catheterization was not performed because it has been documented that peripheral venous concentrations of indocyanine green equal those in the arterial circulation.\(^7\)

Experiments were initiated by administering patients a 12-mg priming dose of indocyanine green followed by a 0.55-mg/min continuous infusion of the dye. After a 15-minute equilibration period, blood was sampled every 8 minutes from the contralateral arm. After four samples had been drawn, the patients were administered subcutaneous injections on separate days in a random sequence with either octreotide (0.4 \(\mu\)g/kg), or dihydroergotamine (7.0 \(\mu\)g/kg), or placebo (normal saline). They were then fed a 400-kcal liquid breakfast (41% carbohydrate, 39% protein, and 20% fat). Indocyanine green was continuously administered, and blood was sampled as described above for an additional 64 minutes after the injection of the drug. Indocyanine green concentrations were measured spectrophotometrically at 800 nM (Model 1001 spectrophotometer, Milton Roy Co., Rochester, N.Y.); serum obtained from blood drawn before the infusion was used to correct for background absorbance. Splanchnic blood flow was estimated by dividing the indocyanine green infusion rate by the steady-state concentration of dye corrected for the assumed hepatic extraction ratio (0.8) as follows:

\[
\text{Splanchnic blood flow} = \frac{0.55 \text{ mg/min}}{0.8 \text{ (Indocyanine green)}} \times \frac{1}{1 - \text{Hematocrit level}}
\]

Splanchnic vascular resistance was calculated by dividing the mean blood pressure by the estimated splanchnic blood flow.

Five autonomic neuropathy patients participated in the indocyanine green clearance protocol on 3 separate days, one for each of the drug treatments described above. Two additional patients participated only twice and were given placebo on 1 day and octreotide on another. Dihydroergotamine was not administered to the latter individuals because they had symptoms suggestive of coronary vascular disease. The control subjects participated in the indocyanine green clearance study only once. They were given the 400-kcal liquid breakfast but were not administered octreotide or dihydroergotamine.

**Measurement of Forearm Blood Flow**

Forearm blood flow was measured by plethysmography with mercury-filled Silastic strain gauges. The plethysmograph (EC-4, D.E. Hokanson, Issaquah, Wash.) was calibrated to convert the changes in limb volume that resulted from occlusion of venous outflow (by applying a pressure of 50 mm Hg proximal to the strain gauge) to blood flow expressed as milliliters of blood flow per 100 milliliters of forearm volume.\(^8\) Pressure was applied for 8 seconds of a 19-second cycle using a timed cuff inflator (manufactured by John Dyson, University of Iowa, Iowa City). Circulation in the hand was excluded by applying a suprasystolic pressure to the wrist. The arm was flexed at the elbow and elevated above the right atrium to ensure venous emptying. Blood flow was calculated by taking the average of five consecutive readings. Forearm vascular resistance was calculated by dividing the mean arterial blood pressure by the forearm blood flow.

**Effect of food ingestion, octreotide, and dihydroergotamine on forearm vascular resistance.** The design of the forearm vascular resistance study was the same as that of the indocyanine green protocol, except that forearm blood flow rather than splanchnic flow was measured at 8-minute intervals. Drugs were injected and food administered after four baseline readings had been obtained as previously described. All the autonomic neuropathy patients participated in this protocol. Eight were studied semirecumbent in a bed with its head elevated to 30\(^\circ\). The five patients with supine hypertension could not be studied in this posture because they were at risk for developing excessive elevations in their blood pressure after the administration of octreotide. Therefore, all studies in these individuals were performed while they were sitting in a chair. Octreotide, dihydroergotamine, and placebo were administered on separate days according to a random sequence. All 13 patients were injected with octreotide and a placebo. Only nine patients were administered dihydroergotamine; four were not given this agent because of suspected coronary vascular disease.

**Effect of octreotide and dihydroergotamine on forearm vascular resistance in fasting patients.** This study was identical to that just described, except the liquid breakfast was omitted. Eleven patients participated in this protocol. Nine received all three treatments.
(octreotide, dihydroergotamine, and placebo); two received octreotide and placebo only.

Measurement of Cardiac Output

Cardiac output was measured by two-dimensional and Doppler echocardiography by multiplying the mean velocity integral of the blood flow by the cross-sectional area of the left ventricular outflow tract with the following formula: cardiac output is equal to π (multiplied by radius squared) multiplied by mean velocity integral multiplied by heart rate. Patients were studied fasting in the morning while flat on their back on a tilt table adjusted to 15° to avoid excessive elevations in blood pressure as described above (see measurement of superior mesenteric artery flow). Eleven patients participated in this protocol, six with idiopathic autonomic neuropathy and five with diabetic autonomic neuropathy. Patients participated in this protocol on 1 day only. Cardiac output and blood pressure were measured simultaneously before and 10 minutes after an injection of octreotide (0.4 μg/kg).

Statistical Methods

Plasma norepinephrine concentrations and performance on autonomic function tests were assessed by analysis of variance. The effect of octreotide on cardiac output and splanchnic blood flow (as calculated from steady-state indocyanine green concentrations) was analyzed by the paired t test. Data from all other protocols were analyzed by repeated measures analysis of variance.15

Results

Effect of Octreotide and Dihydroergotamine on the Hemodynamic Response to Eating and Indocyanine Green Clearance

Food ingestion caused a marked decrease in mean blood pressure (from 98±6 to 70±6 mm Hg) in the patients with autonomic neuropathy. The hypoten-
autonomic neuropathy \((p<0.001)\) and from 97±9 to 125±10 mm Hg in those with diabetic autonomic neuropathy \((p<0.001)\) (Figures 2 and 3). Forearm vascular resistance similarly increased after octreotide from 19.1±1 to 27.2±3.8 \((p<0.01)\) in patients with idiopathic autonomic neuropathy and from 25.2±3.9 to 41.0±6.8 in diabetic autonomic neuropathy \((p<0.01)\). Octreotide had no effect, however, on forearm blood flow in this protocol.

**Effect of Octreotide and Dihydroergotamine on Forearm Vascular Resistance in Fasting Patients**

When patients were fasting, octreotide administration increased mean blood pressure, decreased forearm blood flow by approximately 15% \((p<0.01)\), and increased forearm vascular resistance (Figure 4). Dihydroergotamine similarly increased mean blood pressure and forearm vascular resistance (Figure 5), whereas placebo administration affected none of these parameters (data not shown). Octreotide increased forearm vascular resistance similarly whether patients were fasting or fed (Figure 4). Dihydroergotamine, by contrast, had variable effects on forearm vascular resistance depending on the nutritional status of the patients. When patients were fasting, dihydroergotamine increased forearm vascular resistance, but this effect was not evident when the injection was followed by a liquid breakfast that led to a transient decrease in forearm vascular resistance despite the dihydroergotamine (Figure 5).

**Effect of Octreotide on Cardiac Output and Systemic Vascular Resistance**

Octreotide increased systolic, mean, and diastolic blood pressures in all patients (Table 3). Cardiac index increased after octreotide in five of six patients with idiopathic autonomic neuropathy and in all five patients with diabetic autonomic neuropathy (Figure 6). The mean cardiac output for the two groups of patients was 4.2±0.3 before octreotide and 5.1±0.3 l/min after octreotide administration \((p<0.001, Table 3)\). Systemic vascular resistance increased from 21.2±2.0 to 24.9±2.6 l/min/mm Hg after octreotide administration in the patients with idiopathic autonomic neuropathy \((p<0.05)\) but did change significantly in those with diabetic autonomic neuropathy (Table 3).

**Discussion**

Our results indicate that octreotide causes a marked increase in splanchnic vascular resistance in patients with autonomic neuropathy. This action of the drug probably explains its therapeutic effect in patients with postprandial hypotension.12 Although a large fraction (20–25%) of cardiac output goes to the splanchnic circulation, studying splanchnic vascular tone in humans has been difficult. Indocyanine green clearance provides an index of splanchnic flow because the dye is removed from the circulation exclusively by hepatic mechanisms and the extraction of the dye is nearly complete (averaging 80%) during a single passage through the liver.11–13 Ideally, hepatic vein catheterization should be performed to quantify changes in the extraction ratio of the dye during the course of an experiment. This is not always feasible, however, particularly in patients, such as those in the present study, who are elderly and debilitated and unwilling to participate in invasive protocols. When hepatic vein catheterization cannot be performed, the clearance of indocyanine green provides only an approximation of splanchnic blood flow, accurate to the extent that the extraction ratio of the dye approaches the estimated ratio of 0.8. Given these assumptions, our data indicate that octreotide causes a 22% reduction of splanchnic blood flow in patients with autonomic neuropathy. This result agrees favorably with those previously obtained in normal subjects, in whom indocyanine green clearance was
measured with hepatic vein catheterization, documenting that both somatostatin and octreotide cause a 25–35% decrease in splanchnic blood flow.

Octreotide increased forearm and splanchnic vascular resistance in patients with autonomic neuropathy. The effect of octreotide was the opposite to that of food ingestion for both vascular beds. Thus, forearm vascular resistance increased 40% when octreotide was administered before food ingestion; by contrast, food ingestion alone (placebo treatment, Figure 2) decreased forearm vascular resistance by nearly 50%. We previously reported that food ingestion decreased systemic vascular resistance in a patient with severe postprandial hypotension and suggested that vasoactive gut peptides released into the circulation during eating mediated this effect. This hypothesis was based on the observation that somatostatin, which is known to inhibit the secretion of most gut peptides, prevents postprandial hypotension. This theory, however, fails to explain a number of observations in the present study. First, octreotide not only prevented the decrease in forearm vascular resistance during the postprandial period, it actually increased the latter by 40%. This effect of octreotide was observed even when patients were fasting (Figure 4) and presumably not secreting the putative vasodilating peptide. Moreover, patients with diabetic autonomic neuropathy who did not have a decrease in blood pressure or forearm vascular resistance after eating (therefore, exhibiting no

Figure 2. Plots of effect of octreotide on mean blood pressure, forearm blood flow, and vascular resistance in patients with idiopathic autonomic neuropathy. Arrows indicate that patients (n=8) were administered either octreotide (0.4 μg/kg, ●) or placebo (○) immediately before a 400-kcal liquid breakfast. Data represent mean±SEM. Mean blood pressure and forearm vascular resistance were higher after octreotide than after placebo administration (⁎⁎ p<0.005).

Figure 3. Plots of effect of octreotide on mean blood pressure, forearm blood flow, and vascular resistance in patients with diabetic autonomic neuropathy. Arrows indicate that patients (n=5) were administered either octreotide (0.4 μg/kg, ●) or placebo (○) in addition to insulin immediately before a 400-kcal liquid breakfast. Data represent mean±SEM. Mean blood pressure and forearm vascular resistance were higher after octreotide than after placebo administration (⁎⁎ p<0.01).
evidence of generalized vasodilation during the postprandial period) nevertheless showed a typical pressor response to octreotide (Figure 3). These observations, taken together, suggest that the pressor effect of octreotide in patients with autonomic neuropathy is not secondary to the suppression of a vasodilating factor but rather represents a direct vascular effect of the drug.

Dihydroergotamine was included in this study because pretreatment of patients with this agent potentiates the pressor response to octreotide. We have interpreted this observation to mean that the two drugs may act on different vascular beds, and accordingly, the present results document that octreotide increases splanchnic vascular resistance but dihydroergotamine does not. Forearm vascular resistance, by

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Plot of effect of food ingestion on the vascular response to octreotide. Arrow indicates that patients (n=11) were administered octreotide (0.4 μg/kg) with (●) or without (○) a 400-kcal liquid breakfast. Data represent the mean±SEM. Octreotide increased forearm vascular resistance significantly over baseline (**p<0.01), and forearm vascular resistance was higher after octreotide than after placebo administration (†p<0.01).

![Figure 5](http://circ.ahajournals.org/)

**Figure 5.** Plot of effect of food ingestion on the vascular response to dihydroergotamine. Arrows indicate that patients (n=9) were administered dihydroergotamine subcutaneously (7 μg/kg) with (●) or without (○) food ingestion. All data represent the mean response±SEM. Dihydroergotamine administration increased forearm vascular resistance significantly over baseline (**p<0.005). Forearm vascular resistance was higher after dihydroergotamine than after placebo administration (†p<0.01) only when the patients were fasting.

### TABLE 3. Effect of Octreotide on Blood Pressure, Cardiac Output, and Systemic Vascular Resistance

<table>
<thead>
<tr>
<th></th>
<th>Before octreotide</th>
<th>After octreotide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic blood pressure (mm Hg)</strong></td>
<td>IAN 116±7</td>
<td>155±10*</td>
</tr>
<tr>
<td></td>
<td>DAN 113±9</td>
<td>143±10*</td>
</tr>
<tr>
<td></td>
<td>All patients 115±5</td>
<td>150±7†</td>
</tr>
<tr>
<td><strong>Mean blood pressure (mm Hg)</strong></td>
<td>IAN 91±8</td>
<td>119±5*</td>
</tr>
<tr>
<td></td>
<td>DAN 94±5</td>
<td>112±7*</td>
</tr>
<tr>
<td></td>
<td>All patients 92±5</td>
<td>116±4†</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure (mm Hg)</strong></td>
<td>IAN 70±5</td>
<td>90±3*</td>
</tr>
<tr>
<td></td>
<td>DAN 74±3</td>
<td>91±3*</td>
</tr>
<tr>
<td></td>
<td>All patients 72±3</td>
<td>90±2†</td>
</tr>
<tr>
<td><strong>Heart rate (beats/min)</strong></td>
<td>IAN 74±4</td>
<td>71±3</td>
</tr>
<tr>
<td></td>
<td>DAN 93±7</td>
<td>83±4</td>
</tr>
<tr>
<td></td>
<td>All patients 82±5</td>
<td>76±3</td>
</tr>
<tr>
<td><strong>Cardiac output (l/min)</strong></td>
<td>IAN 4.4±0.4</td>
<td>5.0±0.5*</td>
</tr>
<tr>
<td></td>
<td>DAN 3.8±0.4</td>
<td>5.1±0.4*</td>
</tr>
<tr>
<td></td>
<td>All patients 4.2±0.3</td>
<td>5.1±0.3†</td>
</tr>
<tr>
<td><strong>Systemic vascular resistance (l/min/mm Hg)</strong></td>
<td>IAN 21.2±2.0</td>
<td>24.9±2.6‡</td>
</tr>
<tr>
<td></td>
<td>DAN 25.3±2.1</td>
<td>22.2±2.0</td>
</tr>
<tr>
<td></td>
<td>All patients 23.0±2.0</td>
<td>23.7±2.1</td>
</tr>
</tbody>
</table>

Data are mean±SEM.
IAN, idiopathic autonomic neuropathy (n=6); DAN, diabetic autonomic neuropathy (n=5).
*p<0.02, †p<0.001, ‡p<0.05, vs. before octreotide.
contrast, was increased by both drugs, although dihydrowergotamine showed this effect only when patients were fasting. Because food ingestion counteracts the effect of dihydrowergotamine on forearm vascular resistance, it generally fails to prevent postprandial hypotension.8,19 The vasoconstrictor effect of octreotide, by contrast, is evident both before and after eating; in fact, food ingestion may even accentuate the effect of the drug on forearm vascular resistance (Figure 4). The postprandial pressor effect of octreotide is a unique action of this drug, sufficiently potent to stabilize even upright blood pressure in some patients with autonomic neuropathy.3

Although octreotide increased forearm and splanchnic vascular resistance, it increased systemic vascular resistance only slightly, and this effect was seen only in those with idiopathic autonomic neuropathy. Thus, octreotide’s vasoconstrictor effect on splanchnic and forearm vessels must be balanced by vasodilator effects on other vascular beds. Octreotide had only minor effects on systemic vascular resistance because the increase in blood pressure caused by the drug was associated with a parallel increase in cardiac output. Although an inotropic effect is possible, it seems more likely that cardiac output increased because of enhanced cardiac filling. A venoconstrictor effect of somatostatin has been described20; perhaps octreotide similarly increases venous tone, thereby enhancing the return of blood to the heart. Because decreased cardiac filling is one of the causes of hypotension in patients with autonomic neuropathy, this action of octreotide may be an important aspect of its therapeutic effect in these patients.

In summary, our data provide evidence that octreotide increases splanchnic vascular resistance in patients with autonomic neuropathy and indicate that this is the likely mechanism for its therapeutic effect in postprandial hypotension. Octreotide also increased forearm vascular resistance, and this effect was evident even when patients were fasting, which suggests a direct vascular effect of the drug unrelated to gut hormone secretion. Last, we demonstrated that the pressor effect of octreotide is associated with increased cardiac output.

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We acknowledge the assistance of Ronald E. Victor, MD, who advised the authors on the measurement of forearm vascular resistance. We also thank Sandoz Pharmaceuticals for providing the octreotide, Mrs. Tanya Shapiro for technical assistance, and the nurses of the General Clinical Research Center of Temple University Hospital who took care of the patients who participated in these studies. Last, we thank Ms. Judy Chapman and Dr. Paul Hshieh of the Department of Medicine, West Virginia University School of Medicine, who performed the statistical analysis of the data.

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![Figure 6](image-url)

**KEY WORDS** • blood flow • splanchnic • vascular resistance • octreotide
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