5-HT, Alpha-Adrenoceptors, and Blood Pressure
Effects of Ketanserin in Essential Hypertension and Autonomic Insufficiency

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SUMMARY The serotonin (5-hydroxytryptamine, 5-HT) antagonist, ketanserin, has a high affinity for 5-HT₂-receptors but it also binds to α₁-adrenoceptors. The compound (10 mg i.v.) lowered mean arterial pressure by 22% ± 2% (mean ± SEM, p < 0.001) in 30 patients with essential hypertension. Measurements of heart rate, cardiac output, cardiac filling pressures, forearm blood flow, renal blood flow, and glomerular filtration rate revealed a hemodynamic pattern compatible with vasodilation of both resistance and capacitance vessels. This was accompanied by moderate reflex cardiostimulation. Ketanserin did not alter the pressor effect of bolus injections of (-)-phenylephrine hydrochloride (25, 50, 100, and 200 μg i.v.). Ketanserin also had a distinct hypotensive effect in four normotensive patients with autonomic insufficiency due to an efferent sympathetic lesion, who were unresponsive to phentolamine (20 mg i.v.). Thus, ketanserin in the dose we have used appears to lower blood pressure independently of α₁-adrenoceptor blockade. On the other hand, in patients with essential hypertension the antihypertensive effect of ketanserin was blunted by pretreatment with prazosin (12 mg/day). Therefore, a certain degree of α₁-adrenergic tone seems to be required for the compound to exert its full antihypertensive action. The findings are indirect evidence for a role of 5-HT in the maintenance of increased vascular resistance in essential hypertension. This may be related, at least in part, to the alleged amplifying effect of 5-HT on α₁-adrenoceptor-mediated vasoconstriction. (Hypertension 6: 100-109, 1984)

KEY WORDS: prazosin • α-adrenoceptors • blood pressure • 5-hydroxytryptamine • ketanserin • prazosin

ALTHOUGH 5-hydroxytryptamine (5-HT, serotonin) was among the first vasoactive amines to be discovered and synthesized, its function in blood pressure regulation is still unclear. Recently, a differentiation between two subtypes of 5-HT-receptors has been made on the basis of radioligand-binding studies using membranes prepared from rat frontal cortex.1 Although specific functions associated with these brain receptors have not been identified, it has been shown that the 5-HT-receptors subserving contraction of vascular smooth muscle cells are of the 5-HT₂-subtype.2-7 A 5-HT₂-receptor antagonist, ketanserin (3-2-[4-(-fluorobenzoyl)-1-piperidinyl]ethyl-2,4-[1H,3H]quinazolinedione, Janssen Pharmaceutica, Beerse, Belgium), devoid of agonist activity, is now available for clinical investigation.4-6 Ketanserin, however, is not fully specific for 5-HT₂-receptors, since it also binds to α₁-adrenoceptors. High concentrations of ketanserin have an antagonistic effect on α₁-adrenoceptor-mediated contractions of isolated arteries and veins.4

Experiments in animals4 and preliminary data in humans5,9 have shown that ketanserin has antihypertensive properties. This may, at least in part, depend on blockade of α₁-adrenoceptors. Indeed, it has been reported that hypotensive doses of ketanserin abolished the pressor response to α₁-agonists in the pithed rat, the anesthetized normotensive rat, and the conscious spontaneously hypertensive rat.10,11

This paper describes the hemodynamic profile of ketanserin’s antihypertensive action in patients with essential hypertension. The possibility that the antihypertensive effect of ketanserin depends on interference with α₁-adrenoceptor-mediated vasoconstriction was tested by comparison of the pressor effects of the α₁-adrenoceptor agonist, phenylephrine, before and after ketanserin and by assessment of the antihypertensive effect of ketanserin after administration of the α₁-adre-
neceptor antagonist, prazosin. The cardiovascular effects of ketanserin were also studied in a small group of patients with autonomic insufficiency, who were unresponsive to the hypotensive action of the nonselective α-adrenoceptor antagonist, phentolamine.

**Methods**

**Patients**

Thirty hypertensive subjects were studied, 21 men and nine women, aged 55 ± 2 years (mean ± SEM; range, 38 to 77 years). The diagnosis of essential hypertension was made by routine screening including intravenous urography. Antihypertensive treatment, if any, was stopped 3 weeks before the study. The patients were admitted to a metabolic ward and received a diet with a fixed sodium and potassium content (50–70 mEq/day and 70–100 mEq/day, respectively). When blood pressure and sodium balance were stable, the patients were investigated in the cardiovascular laboratory after an overnight fast. The use of a new antihypertensive agent was explained to the patients. They all gave their consent to participate in the study. The study protocol was approved by the local hospital ethical committee.

Four patients aged 40–76 years, three women and one man, with chronic autonomic failure of the peripheral type, were also studied. Two patients had idiopathic autonomic neuropathy, one patient had primary amyloidosis, and the remaining patient had amyloidosis of the hereditary type. Clinical signs of involvement of the central nervous system were absent in all. Diagnostic aspects of these patients have been described in detail elsewhere. Incapacitating orthostatic hypotension was the presenting symptom. The systolic pressure overshoot in the Valsalva maneuver was absent, and heart rate did not increase after atropine (2 mg i.v.). Plasma norepinephrine was below the detection limit of 20 pg/ml in two patients and it was 40 and 135 pg/ml in the remainder. It was unresponsive to head-up tilting in all. Thus, the patients had combined efferent sympathetic and parasympathetic lesions. At the time of the study, they had not been on any drug for at least 3 weeks.

**Hemodynamic Measurements**

Arterial pressure was measured directly in a radial artery with a P 23 D Statham transducer and recorded on a direct-writing Hewlett-Packard multigraph. Heart rate was determined from the simultaneously recorded ECG signal. Ketanserin, 10 mg in 20 ml of saline, was infused intravenously in 2 to 3 minutes, and the effects were followed for 2 hours. In the patients with autonomic insufficiency, the effects of ketanserin were compared with those of phentolamine, 20 mg i.v. Ketanserin and phentolamine were given on different occasions at least 2 weeks apart.

More detailed data on central and renal hemodynamics were obtained in 12 hypertensive patients. A Swan-Ganz thermodilution catheter was introduced percutaneously in an antecubital vein and positioned in the pulmonary artery. Triplicate cardiac output (CO) measurements were performed at frequent intervals and integrated mean values for systemic arterial pressure (MAP), right atrial pressure (RAP), pulmonary arterial pressure (PAP), and pulmonary capillary wedge pressure (PCWP) were determined. Pressures and cardiac output were measured with the patients in a supine position, and the transducers were zeroed at midthoracic level. Cardiac output was corrected for body surface area and is expressed per 1.73 m². The following variables were derived: total peripheral resistance is TPR = (MAP – RAP)/CO and pulmonary vascular resistance is PVR = (PAP – PCWP)/CO.

A peripheral vein was cannulated for renal function studies using a constant infusion technique. Effective renal plasma flow and glomerular filtration were estimated by the clearances of 125I-hippuran and 125I-thalamate, respectively. Hemodynamic measurements were made after a 90-minute equilibration period. Renal blood flow (RBF) corrected for 1.73 m² body surface area was calculated using central venous packed cell volume and assuming 75% renal extraction of hippuran. Renal vascular resistance was derived as RVR = MAP/RBF.

The effects of ketanserin on peripheral hemodynamics were studied in a subgroup of eight hypertensive patients. Measurements were taken with the patients supine after resting for at least 30 minutes at a room temperature of 23–25°C and in an air humidity of approximately 50%. Forearm blood flow including hand flow was measured semicontinuously by means of an ECG-triggered venous occlusion plethysmograph (Janssen Scientific Instruments). A mercury-in-Silastic strain gauge was placed around the midforearm, and the arm was elevated so that venous pressure approached zero. Venous occlusion was achieved within 50 msec by inflation of a sphygmomanometer cuff wrapped around the upper arm and attached to a container of compressed air with a pressure valve preset at 50 mm Hg. This occlusion pressure was intermittently applied for a period of three heart beats, with a recovery period of two heart beats. To obtain synchronization between cuff pressure and flow pulse, the occlusion pressure was regulated by means of electromagnetic valves that were triggered by properly delayed impulses derived from the R-top of the electrocardiogram. Forearm blood flow was calculated from the change in forearm circumference during occlusion and was expressed as ml per 100 ml of tissue per minute. Rectal temperature and skin temperature of the forehead and distal, volar surface of digits no. 2, 3, and 5 of the nonoccluded arm were recorded by means of telemeters (Yellow Springs Instruments, Cleveland, Ohio).

**Phenylephrine Injections**

In seven patients with hypertension, bolus injections of (-)-phenylephrine hydrochloride (25, 50, 100, and 200 µg) in random order, were flushed into the circulation through a cannula in an antecubital vein, before and during ketanserin infusion. Intraarterial pressure...
and the electrocardiogram were simultaneously recorded on a multichannel ink-jet writer (Mingograph Siemens, Elema, Solna, Sweden) at a paper speed of 100 mm/sec. The interval between the injections was 10 minutes. After the first series of injections had been finished, a loading dose of 10 mg ketanserin was infused intravenously in 2 or 3 minutes followed by a sustaining infusion of 2 mg/hour. According to the manufacturer, in this way a stable plasma level of about 80 ng/ml is reached within 15 minutes. A second series of phenylephrine bolus injections was then given. The 200 µg dose of phenylephrine was used for determination of baroreflex sensitivity. Measurements covered the period from the onset of the rise in arterial pressure until pressure had reached its peak level. Baroreflex sensitivity was expressed as the slope of the regression line relating RR-interval to the systolic pressure of the preceding heart beat. The result was accepted only when the correlation coefficient was greater than 0.75, with a p value of less than 0.05. In one patient these conditions were not met.

A third series of phenylephrine injections was given to five patients after they had been treated with prazosin, 4 mg orally three times a day for 2 days. Phenylephrine was injected 60–90 minutes after the morning dose of prazosin.

Pretreatment with Prazosin and Furosemide

Fourteen patients with essential hypertension, in whom the effects of a first dose of ketanserin (10 mg i.v.) had been followed for 2 hours, were randomly assigned to two treatment modalities. Eight patients were treated with prazosin (4 mg three times a day) for 1 week, and the effects of a second dose of ketanserin (10 mg i.v.) were studied 60–90 minutes after the morning dose of prazosin. Six patients were treated with furosemide (40 mg daily) and after 1 week a second dose of ketanserin (10 mg i.v.) was administered.

Analytical Procedures

For determinations of plasma renin and aldosterone, arterial blood was collected in chilled tubes containing disodium ethylenediaminetetraacetate (EDTA) in a final concentration of 2 mg/ml of blood, and stored on ice for no longer than 60 minutes until centrifugation at 5,000 rpm for 15 minutes at 4°C to separate the plasma. Plasma was stored at −20°C. Active renin was measured by radioimmunoassay as described previously. Semipurified human kidney renin (MRC standard no. 68/356, WHO International Laboratory for Biological Standards and Control, London, England) was used as a standard, and results are expressed as microunits of this standard per milliliter of plasma.
The normal range in our laboratory is 15–40 μU/ml. Plasma aldosterone was also measured by radioimmunoassay. The normal range is 40–180 pg/ml. For determination of plasma norepinephrine, 10 ml of arterial blood was collected into a chilled tube containing 143 USP units lithium heparin and 15 mg glutathione in 200 μl distilled water. After centrifugation, the plasma was deproteinized with trichloroacetic acid. The precipitate was removed by centrifugation at 8000 rpm for 15 minutes and the supernatant was stored at −20°C. Norepinephrine was measured by a radioenzymatic method, in which norepinephrine is quantitatively converted to 3H-epinephrine in the presence of phenylethanolamine-N-methyltransferase using 3H-S-adenosyl-L-methionine as a 3H-methyl group donor. All samples were assayed in duplicate, both with and without the addition of norepinephrine as the internal standard. The normal range is 150–450 pg/ml.

Statistical Analysis

Data are given as means ± SEM. Plasma levels of renin were not distributed normally. Mean values and standard errors were calculated after logarithmic transformation. Student's t tests for paired and unpaired data were used. Statistical significance was taken to be p < 0.05.

Results

Studies in Essential Hypertension

Systemic, Central, and Peripheral Hemodynamics and Plasma Norepinephrine

In 30 patients, arterial pressure fell from 177 ± 5/86 ± 3 mm Hg before ketanserin to 139 ± 6/68 ± 3 mm Hg (p < 0.001) after ketanserin injection. Heart rate rose from 68 ± 2 to 78 ± 3 bpm (p < 0.01). Fifteen minutes after ketanserin, arterial pressure was still low, 147 ± 6/72 ± 3 mm Hg (p < 0.001 for difference from baseline), but heart rate had returned to 73 ± 3 bpm. The effects on arterial pressure, heart rate, and plasma norepinephrine, which were followed for 2 hours in 20 patients, are shown in Figure 1. After 2 hours, mean arterial pressure was still significantly below baseline (p < 0.05) and norepinephrine was still elevated (p < 0.05), whereas heart rate had already returned to baseline.

The fall in arterial pressure after ketanserin was caused by a fall in total peripheral resistance (Figure 2). Cardiac output rose from 4.35 ± 0.26 liter/min before ketanserin to 4.68 ± 0.26 liter/min (p < 0.01) 5 minutes after the ketanserin injection. Thereafter, cardiac output fell, and after 90 minutes it was 4.08 ± 0.23 liter/min, which was even below baseline (p < 0.05). Stroke volume was 68 ± 4 ml before ketanserin. It was not altered 5 minutes after ketanserin but it fell to 61 ± 3 ml after 90 minutes (p < 0.01 for difference from baseline). Right atrial pressure, pulmonary arterial pressure, and pulmonary capillary wedge pressure were also lowered (Figure 3). Pulmonary vascular resistance was not altered. Forearm blood flow and digital skin temperature increased markedly after ketanserin (Table 1). Rectal temperature and skin temperature of the forehead remained constant.

Renal Hemodynamics, Plasma Renin, and Aldosterone

The pattern of flow and resistance changes induced by ketanserin in the renal vascular bed resembled the changes in the systemic circulation (Figure 4). Renal blood flow was 736 ± 44 ml/min before ketanserin and rose to 767 ± 51 ml/min (p < 0.05) 15 minutes after the drug. Glomerular filtration rate was 90 ± 5 ml/min before ketanserin and remained unchanged de-
FIGURE 3. Effects of ketanserin (10 mg i.v.) on central hemodynamics in 12 patients with essential hypertension. After 120 minutes, all changes were still significant at $p < 0.05$.

Despite the decrease in arterial pressure. Plasma renin rose from 9.4 $\mu$U/ml (antilog of arithmetic mean after logarithmic transformation of data) before ketanserin to 17 $\mu$U/ml ($p < 0.01$) 30 minutes after the drug. Plasma aldosterone did not change; it was 102 ± 15 pg/ml before ketanserin and 92 ± 14 pg/ml after 30 minutes.

Responses to Bolus Injections of Phenylephrine

From the start of the injection until changes had returned to baseline pulsatile and mean arterial pressures and the RR-interval of the ECG were analyzed beat to beat. Figure 5 shows an example. Mean arterial pressure and the subsequent RR-interval (pulse interval) were used for constructing log dose-response curves. As shown in Figure 6, the changes in mean arterial pressure and pulse interval were not modified by ketanserin. However, treatment with prazosin competitively antagonized the responses, as indicated by a parallel shift of the dose-response curve to the right (Figure 7). Baroreflex sensitivity was not modified by ketanserin. It was 8.82 ± 1.71 msec/mm Hg before ketanserin and 9.03 ± 1.52 msec/mm Hg after the drug.

Effects of Pretreatment with Prazosin or Furosemide

Mean arterial pressure was 114 ± 8 mm Hg in the patients who were to be treated with prazosin and 116 ± 6 mm Hg in the patients to be treated with furosemide. After 1 week of treatment, mean arterial pressure was 103 ± 6 mm Hg in the prazosin group ($p < 0.05$ for difference from the value before treatment) and 102 ± 4 mm Hg in the furosemide group ($p < 0.05$). Body weight did not change with prazosin and fell by 2.1 ± 0.3 kg with furosemide ($p < 0.01$). The blood pressure response to ketanserin was blunted by pretreatment with prazosin and was not affected by pretreatment with furosemide (Figure 8).

Studies in Autonomic Insufficiency

Arterial pressure fell from 128 ± 8/66 ± 3 mm Hg before ketanserin to 95 ± 4/56 ± 3 mm Hg ($p < 0.01$ after 15, 30, and 45 minutes).
TABLE 1. Effects of Ketanserin (10 mg i.v.) on Systemic and Regional Hemodynamics (mean ± SEM) in Eight Patients with Essential Hypertension

<table>
<thead>
<tr>
<th>Time (min) before and after ketanserin administration</th>
<th>~5</th>
<th>0</th>
<th>2.5</th>
<th>5</th>
<th>10</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>111±6</td>
<td>115±5</td>
<td>99±6†</td>
<td>101±6†</td>
<td>105±6*</td>
<td>106±6*</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>65±4</td>
<td>65±4</td>
<td>72±3†</td>
<td>70±3*</td>
<td>67±4</td>
<td>65±4</td>
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<tr>
<td>Forearm blood flow (ml/min/100 ml)</td>
<td>3.6±0.2</td>
<td>3.7±0.2</td>
<td>6.5±0.5†</td>
<td>6.3±0.6†</td>
<td>5.4±0.5*</td>
<td>4.4±0.6*</td>
</tr>
<tr>
<td>Digital skin temperature (°C)</td>
<td>31.3±0.8</td>
<td>31.2±0.8</td>
<td>31.8±0.9</td>
<td>33.2±0.6*</td>
<td>33.3±0.6*</td>
<td>33.6±0.8*</td>
</tr>
</tbody>
</table>

*p < 0.05.  
†p < 0.01.

0.001) after the ketanserin injection (Table 2). In contrast, 20 mg phentolamine i.v. had no effect on arterial pressure in these patients. With both drugs, heart rate did not change.

Discussion

Cardiovascular and Hormonal Effects of Ketanserin

The profile of ketanserin’s hemodynamic effects is compatible with combined arteriolar and venous dilation. Systemic arterial pressure, total peripheral resistance, and cardiac filling pressures were lowered. Part of the decrease in total peripheral resistance was caused by renal vasodilatation. Forearm resistance was also reduced, and this reduction appeared out of proportion as compared to the overall reduction in vascular resistance. The hand was included in our semicontinuous measurements of forearm flow so that changes in hand skin flow have influenced the results. Indeed, our thermographic studies showed that digital skin flow was increased by ketanserin, presumably by opening of arteriovenous shunts, which are densely innervated by sympathetic nerves and possibly also by serotonergic fibers. It is worth mentioning that forehead skin flow, as estimated by skin temperature

![Figure 5](http://hyper.ahajournals.org/)
measurements, was not increased by ketanserin. This contrasts with the rise of forehead temperature after hydralazine.\textsuperscript{21}

The fall in arterial pressure was associated with increments in heart rate and cardiac output, probably by baroreflex-mediated withdrawal of vagal tone and increase in sympathetic activity.\textsuperscript{22} The increased sympathetic activity was reflected by a rise in plasma norepinephrine. Despite continued sympathetic stimulation, cardiac output returned to its initial level. This may have been due to the gradual decrease in cardiac filling pressures. For a given effect on arterial pressure, the increase in heart rate after ketanserin was less than with drugs like hydralazine and diazoxide,\textsuperscript{21, 22} which have their predominant effect on the resistance vessels.

Sympathetic stimulation may have contributed to the observed rise in plasma renin. It may be of interest that plasma aldosterone did not change after ketanserin. From studies with isolated rat glomerulosa cells it is known that 5-HT has direct aldosterone-stimulating properties.\textsuperscript{23} Suppression of aldosterone was found in patients with idiopathic aldosteronism after administration of the antiseroetonergic agent cyproheptadine.\textsuperscript{24} The divergent responses of plasma renin and aldosterone after ketanserin in our patients suggest a suppressive effect of 5-HT blockade on aldosterone secretion but further studies are needed to clarify this point.

**Mechanism of Antihypertensive Action of Ketanserin**

Ketanserin has been characterized as a selective \textsuperscript{3}H-ligand for 5-HT$_2$-binding sites in brain.\textsuperscript{2} These binding sites probably differ\textsuperscript{7} from the D- and M-types of 5-HT-receptors postulated by Gaddum and Picarelli.\textsuperscript{25} The close connections between the central serotonergic neuronal system and the pathways of catecholaminergic neurons suggest a role for 5-HT in cardiovascular control, but both pharmacological and surgical
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FUROSEMIDE • before o after PRAZOSIN

CHANCE IN MEAN ARTERIAL PRESSURE mmHg

CHANCE IN HEART RATE beats/min

KETANSERIN

TIME (min)

FIGURE 8. Effects of pretreatment with furosemide or prazosin on the antihypertensive action of ketanserin (10 mg i.v.) in, respectively, six and eight patients with essential hypertension. The decrements in arterial pressure after ketanserin were smaller (p < 0.01) throughout the observation period in the prazosin-treated patients.

TABLE 2. Effects of Ketanserin (10 mg i.v.) and Phentolamine (20 mg i.v.) on Systemic Arterial Pressure and Heart Rate in Four Patients with Autonomic Insufficiency

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Ketanserin time (min)</th>
<th>Phentolamine time (min)</th>
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<tr>
<td></td>
<td>-5 0 2.5 5 10 15</td>
<td>-5 0 2.5 5 10 15</td>
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Systolic arterial pressure (mm Hg)

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<td>-5 0 2.5 5 10 15</td>
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Diastolic arterial pressure (mm Hg)

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<th>Case no.</th>
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<th>Phentolamine</th>
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<td>-5 0 2.5 5 10 15</td>
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Heart rate (bpm)

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<th>Case no.</th>
<th>Ketanserin</th>
<th>Phentolamine</th>
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<td>-5 0 2.5 5 10 15</td>
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*p < 0.01.
manipulations of this central serotonergic system have yielded conflicting results. From animal studies, ketanserin appears to be more potent as a serotonin antagonist in the periphery than in the central nervous system.

The peripheral effects of 5-HT are notoriously variable. 5-HT can cause either contraction or relaxation of vascular smooth muscle cells depending on the anatomical origin of the blood vessel studied, the species, experimental conditions, and concentration of the monoamine. Apart from its direct vasoconstrictor effect, 5-HT also amplifies the responses to endogenous vasopressor substances such as norepinephrine and angiotensin II. This could be a conceptual framework for visualizing how 5-HT may contribute to the elevated vascular resistance in essential hypertension. The available pharmacological evidence, which includes experiments using ketanserin as a 5-HT-antagonist, indicates that the 5-HT-receptors subserving vascular smooth muscle contraction are of the 5-HT_1-receptor subtype. This is not only true for the direct vasoconstrictor effect of 5-HT but probably also for its indirect effect through amplification of the responses to norepinephrine.

In anesthetized normotensive rats and in conscious spontaneously hypertensive rats, doses of ketanserin required to lower blood pressure were 25–100 times higher than those required to inhibit the blood pressure response to 5-HT. At such high doses, however, the pressure responses to α-adrenoceptor agonists were also blocked. It is unlikely that ketanserin (10 mg i.v.) caused α_1-adrenoceptor blockade in our patients, since the pressor responses to bolus injections of phenylephrine were not altered. This contrasted with the shift of the dose-response curve to the right that was observed after treatment with the α_1-adrenoceptor antagonist, prazosin. Heart rate was reduced by bolus injections of phenylephrine due to a baroreflex-mediated increase in vagal tone. The relationship between the responses of pressure and heart rate to phenylephrine was not altered by previous administration of ketanserin, which suggests that the sensitivity of the baroreflex was not affected by this drug.

That ketanserin can lower blood pressure independently of α-adrenoceptor blockade was substantiated in our patients with autonomic insufficiency. The non-selective α-adrenoceptor antagonist phentolamine (20 mg i.v.) had no effect on blood pressure and heart rate in these patients, whereas this dose is known to cause hypotension and tachycardia in normal individuals. This confirmed the presence of an effenter sympathetic lesion in our patients resulting in a low occupancy of the α_1- and α_2-adrenoceptors. Still, ketanserin had a distinct hypotensive effect in these patients.

Pretreatment with prazosin attenuated the antihypertensive effect of ketanserin in our hypertensive patients. Pretreatment with furosemide, which had an effect on blood pressure comparable to that of prazosin, did not affect the response to ketanserin. Perhaps a certain degree of endogenous tone on vascular α_1-adrenoceptors is required for ketanserin to exert its full antihypertensive action. This is in accord with the contention that 5-HT_2-receptor stimulation is capable of amplifying the pressor response to norepinephrine.

We conclude that the antihypertensive action of ketanserin that we have observed is not caused by blockade of α_1-adrenoceptors. The pharmacological evidence obtained so far supports that this effect depends on blockade of vascular 5-HT_1-receptors. Our findings are therefore indirect evidence for a role of 5-HT in the maintenance of an increased vascular resistance in essential hypertension.

References


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