Role of Endothelium-Derived Prostanoid in Angiotensin-Induced Vasoconstriction

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To test the hypothesis that prostanoids contribute to angiotensin II-induced vascular contraction, we compared the effect of angiotensin II on isometric tension development by rings of descending thoracic aorta bathed in Krebs' bicarbonate buffer with and without indomethacin (10 μM) to inhibit cyclooxygenase, CGS13080 (10 μM) to inhibit thromboxane A2 synthesis, or SQ29548 (1 μM) to block thromboxane A2/prostaglandin endoperoxide receptors. The comparisons were made in rings of aorta taken from normotensive rats and from rats with aortic coarctation-induced hypertension at 12 days and 90-113 days after coarctation. These rings released thromboxane B2, which was found to be endothelium dependent, increased in hypertensive rats, and stimulated by angiotensin II (10^-6 M) in normotensive rats and in hypertensive rats at 12 days after coarctation. The angiotensin II (10^-6 to 10^-5 M)-induced contraction of aortic rings was increased by about 30% at 12 days after coarctation and decreased at 90-113 days after coarctation. Removal of the endothelium increased the contractile effect of angiotensin II (10^-6 M) in aortic rings of normotensive rats and hypertensive rats at 90-113 days after coarctation but decreased the effect in aortic rings of hypertensive rats at 12 days after coarctation. In rats at 12 days after coarctation, the angiotensin II (10^-6 M)-induced contraction of aortic rings with endothelium was attenuated by indomethacin and SQ29548 but not by CGS13080. These data suggest that a prostanoid-mediated and endothelium-dependent mechanism of vasoconstriction contributes to the constrictor effect of angiotensin II in aortic rings of rats in the early phase of aortic coarctation-induced hypertension. (Hypertension 1991;18:158-164)

Angiotensin II stimulates synthesis of prostaglandin I2 (PGI2) and E2 (PGE2), and these vasodilatory prostanoids, in turn, interfere with the expression of angiotensin II-induced vasoconstriction.1 It is well established that this type of angiotensin II–prostanoid interaction contributes prominently to homeostatic mechanisms that defend against the vasoconstrictor and pressor actions of angiotensin II in settings featuring increased activity of the renin-angiotensin system.1

Several recent studies have suggested a second type of angiotensin II–prostanoid interaction, one that links vasoconstrictor prostanoids such as thromboxane A2 (TxA2) or the prostaglandin endoperoxides to the mechanisms of angiotensin II–dependent hypertension. For example, the increase of blood pressure produced by chronic infusion of angiotensin II in saline-drinking rats was attenuated by concomitant treatment with a blocker of the receptors shared by TxA2 and the prostaglandin endoperoxides,2 just as the pressor response to short-term infusion of angiotensin II was attenuated by pretreatment with either a blocker of TxA2/prostaglandin endoperoxide receptors or an inhibitor of thromboxane synthase.3 Moreover, treatment with a blocker of TxA2/prostaglandin endoperoxide receptors was reported to lower the blood pressure of rats with established angiotensin II–salt-induced hypertension4 as well as that of rats in the early stage of the hypertension produced by complete ligation of the aorta between the renal arteries,5 a model of hypertension that is angiotensin dependent in the early stage and angiotensin independent in the late stage.

This study was undertaken to investigate the interaction of angiotensin II and vasoconstrictor prostanoids in relation to the mechanism of angiotensin II–induced contraction of vascular smooth muscle in normotensive and hypertensive rats. We studied the effect of angiotensin II on isometric tension development by rings of thoracic aorta taken from sham-operated rats and from rats with aortic coarctation-induced hypertension; the effect of angiotensin II was studied in the absence and the presence of a
cyclooxygenase inhibitor, a thromboxone synthase inhibitor, or a blocker of TxA2/prostaglandin endoperoxide receptors.

Methods

Experimental Drugs

Angiotensin II ([(Ile2] angiotensin II), phenylephrine, acetylcholine, and indomethacin, an inhibitor of cyclooxygenase, were purchased from Sigma Chemical Co., St. Louis, Mo. U46619 (15S-hydroxy-11α,9α[epoxy-methan]prosta-5z-dienoic acid), a prostaglandin endoperoxide analogue that is an agonist for TxA2 receptors,6 was purchased from Cayman Chemical, Ann Arbor, Mich. SQ29548 (1S-[1α,2β(25z),3β,4α]-7-[3-(2-phenylamino)carbonyl]hydrazino methyl]-7-oxabicyclo(2.2.1)hept-2-yl]-5-heptenoic acid, a blocker of TxA2/prostaglandin endoperoxide receptors,7 was obtained from Squibb Institute for Medical Research, Princeton, N.J. CGS13080 (imidazo[1,5-a]pyridine-5-hexanoic acid), an inhibitor of thromboxone synthase,8 was obtained from CIBA-GEIGY, Summit, N.J.

Stock solutions of angiotensin II, phenylephrine, and acetylcholine were prepared in distilled water; solutions of indomethacin and CGS13080 were prepared in 50 mM Na2CO3; and solutions of U46619 and SQ29548 were prepared in a mixture of ethanol and 10 mM Na2CO3 (0.09:0.91 vol/vol). For all the drugs, subsequent dilutions were made using Krebs' bicarbonate buffer.

Animals

Experiments were conducted on male Sprague-Dawley rats (Charles River, Wilmington, Mass.) weighing 300–325 g. The animals were housed in group cages, were given tap water to drink, and were fed a standard chow ad libitum (Ralston Purina, St. Louis, Mo.).

Either aortic coarctation or sham aortic coarctation was produced according to a published procedure4 in rats anesthetized with methoxyflurane (Pitman-Moore, Inc., Washington Crossing, N.J.). Briefly, the abdominal cavity was exposed through a midline incision, a silk ligature (No. 000) was passed around the aorta at a point below the right renal artery and above the left renal artery just below the origin of the superior mesenteric artery, and the aorta was either completely ligated or sham ligated. On the day of the experiment, 7–14 and 90–113 days after aortic coarctation and 9–20 days after sham operation, the right carotid artery of rats anesthetized with sodium pentobarbital (50 mg/kg i.p.) was cannulated with polyethylene tubing (PE-50) connected to a pressure transducer (model P23ID, Statham Division, Gould Inc., Oxnard, Calif.) for recording of mean arterial blood pressure on a polygraph (model 7D, Grass Instrument Co., Quincy, Mass.). After blood pressure measurement, the thoracic cavity was exposed and the descending thoracic aorta was excised for investigation of the contribution of vasconstrictor prostanooids to the mechanism of angiotensin II–induced contraction of aortic rings.

Measurement of Isometric Tension in Vascular Rings

Descending thoracic aortas removed from sham-operated normotensive rats and from rats with aortic coarctation–induced hypertension were immediately transferred to ice-cold Krebs' bicarbonate buffer (composition in mmol/l: NaCl 118.5, KCl 4.7, CaCl2 2.5, KH2PO4 1.2, MgSO4 1.1, NaHCO3 25.0, and dextrose 11.1), were cleared of periadventitial tissue, and were cut transversely using fine-tipped scissors into six ring segments (2.5 mm in length). In some experiments, rings of aorta were denuded of endothelium by gentle rubbing of the intimal surface.

Each ring of aorta was placed inside a water-jacketed 5-ml tissue bath filled with Krebs' bicarbonate buffer (37°C) that was bubbled with 95% O2–5% CO2 and was suspended between two L-shaped stainless steel hooks. The lower hook was attached to a stationary support, the upper hook was attached to a force-displacement transducer (model FT03C, Grass) coupled to a polygraph (model 7D, Grass) for recording of isometric tension. The vascular rings were allowed to equilibrate for 1.5–2.0 hours with changes of buffer at 15-minute intervals and with several adjustments of length until the baseline tension stabilized at 2 g. In preliminary experiments, we found that 2 g of resting tension is optimal for the expression of KCl (120 mM)-induced contraction of rings of aorta obtained from normotensive and hypertensive rats. The presence of functional endothelium was tested in all aortic rings by ascertaining that acetylcholine (5 x 10−7 M) was effective in relaxing the smooth muscle of rings precontracted by phenylephrine (10−6 M). The relaxing response to acetylcholine, expressed as percent inhibition of the phenylephrine-induced contraction, was 50.4 ±2.5%, 35.3 ±2.7% (p<0.05), and 49.3 ±3.8% in aortic rings of sham-operated normotensive rats and of hypertensive rats at 12 days and 90–113 days after aortic coarctation, respectively. Failure of acetylcholine to elicit relaxation of aortic rings previously subjected to rubbing of the intimal surface was taken as proof that the endothelium had been removed.

Experiments were initiated by obtaining in each aortic ring a reference contractile response to a maximally effective concentration of KCl (120 mM). Subsequently, the rings were rinsed with Krebs' bicarbonate buffer and, once the tension had returned to baseline, the responsiveness to angiotensin II, phenylephrine, or U46619 was evaluated. Because rat aortic smooth muscle rapidly develops tachyphylaxis to the contractile effect of angiotensin II,10,11 concentration–response curves to the peptide were generated by challenging each one of several rings from the same aorta with a different concentration of peptide (10−11 to 10−5 M). In this way, each aortic ring was exposed to angiotensin II one time only. Concentration–response curves to phenylephrine (10−8 to 10−5 M) or U46619 (10−8 to 10−5 M) were generated.
in single aortic rings by increasing in a step-wise manner the concentration of agonist. The contractile response to angiotensin II (10^{-6} M) and phenylephrine (10^{-5} to 10^{-3} M) in aortic rings with functional endothelium was studied in the absence and presence of either indomethacin (10 \mu M), CGS13080 (10 \mu M), or SQ29548 (1 \mu M), which were added to the bathing buffer before obtaining the reference contractile response to 120 mM KCl. The magnitude of agonist-induced contraction is expressed as the percentage of the reference aortic contractile response to 120 mM KCl.

**Measurement of Thromboxane B₂ Release From Vascular Rings**

Rings of descending thoracic aorta, with and without endothelium, were obtained as described above from sham-operated normotensive rats and hypertensive rats at 12 days and at 90–113 days after coarctation. Vascular rings were placed in 20-ml flasks containing Krebs’ bicarbonate buffer (2.0 ml), with and without angiotensin II (10^{-6} M), and were incubated for 15 minutes at 37°C in an atmosphere of 95% O₂–5% CO₂ with 100 cycle/min agitation. The amount of TxB₂ released into the medium was measured by enzyme-immunoassay of unextracted samples.¹² The results are expressed as picograms of TxB₂ released during the 15-minute incubation period per milligram of dry tissue.

**Statistical Analysis**

Results are expressed as mean±SEM. Data were analyzed by a one-way or a two-way analysis of variance. If differences were noted, the data were then analyzed by a Newman-Keuls modified t test. The null hypothesis was rejected if the value of p<0.05.

**Results**

The mean arterial pressure of rats with aortic coarctation at 7–14 days (163±2 mm Hg) and at 90–113 days (160±3 mm Hg) after coarctation exceeded (p<0.01) the arterial pressure of sham-operated rats (101±2 mm Hg).

As shown in Figure 1, rings of descending thoracic aorta taken from sham-operated normotensive rats and from hypertensive rats at 12 days and at 90 days after coarctation differed from each other in terms of release of TxB₂ during incubation in Krebs’ bicarbonate buffer, with and without angiotensin II (10^{-6} M). The basal release of TxB₂ from rings of aorta with endothelium was greater (p<0.05) in hypertensive rats at 12 days and at 90 days after coarctation than in normotensive controls. Angiotensin II (10^{-6} M) stimulated (p<0.05) TxB₂ release from aortic rings with endothelium in sham-operated rats and in hypertensive rats at 12 days after coarctation but not in normotensive rats at 90 days after coarctation. After denudation of the aortic endothelium, the basal release of TxB₂ from rings of aorta fell (p<0.05) in normotensive rats and in hypertensive rats at 12 days and at 90 days after coarctation.

Additionally, angiotensin II (10^{-6} M) did not stimulate TxB₂ release from aortic rings denuded of endothelium. In rings of aorta taken from hypertensive rats at 12 days after coarctation, the release of TxB₂ measured during incubation of the rings with angiotensin II (10^{-6} M) (175.6±41.2 pg/mg of tissue) was greatly inhibited (p<0.05) by concurrent incubation with indomethacin (10^{-5} M) (12.4±3.5 pg/mg tissue) or CGS13080 (10^{-3} M) (13.6±2.5 pg/mg tissue).

As shown in Figure 2, rings of descending thoracic aorta taken from sham-operated normotensive rats and from rats in the early and the late phase of aortic coarctation-induced hypertension also differed from each other in terms of contractile responsiveness to angiotensin II. At 12 days after coarctation, the contraction of aortic rings produced by angiotensin II at maximally effective concentrations (10^{-6} and 10^{-5} M) was increased (p<0.05) by about 30% relative to the corresponding data in sham-operated rats. In contrast, at 90–113 days after coarctation, the contraction of aortic rings produced by angiotensin II (10^{-7} to 10^{-5} M) was reduced (p<0.05) relative to the control data in normotensive controls. Importantly, exposure to 120 mM KCl elicited nearly identical increases of isometric tension in rings of aorta taken from sham-operated normotensive rats (1.35±0.07 g) and from hypertensive rats at 12 days (1.33±0.07 g) and at 90–113 days (1.35±0.09 g) after coarctation.

Figure 3 compares in normotensive rats and in rats with aortic coarctation-induced hypertension the effect of angiotensin II (10^{-6} M) on the tone of aortic
Figure 2. Line graph shows concentration-effect curves for angiotensin II-induced contraction of aortic rings taken from sham-operated normotensive rats and rats with aortic coarctation-induced hypertension at 12 days and 90–113 days after coarctation. Each point is mean±SEM of data from six to eight rats. *p<0.05 relative to data in normotensive rats.

Figure 3. Bar graphs compare angiotensin II (10⁻⁶ M)–induced contractions of aortic rings with and without endothelium in sham-operated normotensive rats and rats with aortic coarctation-induced hypertension at 12 days and 90–113 days after coarctation. Values are mean±SEM, and numbers between parentheses represent number of rats. *t*tp<0.05 relative to data in rings with endothelium from normotensive rats, and rings without endothelium from normotensive rats, respectively.

Rings with endothelium and of rings denuded of endothelium. Removal of the aortic endothelium resulted in augmentation (p<0.05) of angiotensin II–induced contraction of aortic rings taken from normotensive controls and from hypertensive rats at 90–113 days after coarctation. In contrast, the angiotensin II–induced contraction of aortic rings taken from hypertensive rats at 12 days after coarctation was diminished in rings denuded of endothelium.

Figure 4 contrasts, in normotensive rats and in rats with aortic coarctation–induced hypertension, the effect of angiotensin II (10⁻⁶ M) on the tone of aortic rings (with endothelium) with and without concurrent exposure to indomethacin (10 μM) to inhibit cyclooxygenase, CGS13080 (10 μM) to inhibit thromboxane synthase, or SQ29548 (1 μM) to block TxA₂ and PG endoperoxide receptors. CGS13080 did not alter contractile responses to angiotensin II in aortic rings from sham-operated normotensive rats or from rats in the early or the late phase of aortic coarctation–induced hypertension. Indomethacin and SQ29548 were both without effect on the angiotensin II–induced contraction of aortic rings from sham-operated rats and hypertensive rats at 90–113 days after coarctation. In contrast, the contractile effect of angiotensin II in aortic rings from hypertensive rats at 12 days after coarctation was reduced (p<0.05) to about 48% and 30% of control by indomethacin and SQ29548, respectively. Importantly, after aortic rings from hypertensive rats at 12 days after coarctation were denuded of endothelium, the contractile response to angiotensin II (10⁻⁶ M) was similar in the absence and the presence of SQ29548 (1 μM) (62.89±2.10% versus 72.12±10.57% of response to 120 mM KCl).

Figure 5 compares in normotensive rats and in rats with aortic coarctation–induced hypertension the effect of phenylephrine (10⁻⁹ to 10⁻³ M) on the tone of aortic rings (with endothelium) with and without concurrent exposure to indomethacin (10 μM), CGS13080 (10 μM) or SQ29548 (1 μM). In all cases, phenylephrine caused concentration-dependent contraction of aortic rings. The concentration–response curve to this agonist in aortic rings taken from normotensive rats was not different from the concentration–response curves obtained in aortic rings from hypertensive rats (12 days after coarctation) with or without concurrent exposure to indomethacin (10 μM), CGS13080 (10 μM) or SQ29548 (1 μM). Aortic rings were obtained from sham-operated normotensive rats and from rats with aortic coarctation–induced hypertension at 12 days and 90–113 days after coarctation. Values are mean±SEM, and numbers between parentheses represent number of rats. *p<0.05 relative to control.
hypertensive rats at either 12 days or 90–113 days after coarctation. Neither indomethacin nor SQ29548 affected the phenylephrine-induced contraction of aortic rings from normotensive or hypertensive rats.

Figure 6 contrasts the effect of U46619 (10⁻⁹ to 10⁻⁵ M), a synthetic agonist for TxA₂ and prostaglandin endoperoxide receptors, on the tone of rings of aorta (with endothelium) taken from sham-operated rats and from rats with aortic coarctation-induced hypertension. U46619 elicited concentration-dependent contraction of aortic rings, which was similar in rings taken from sham-operated rats and from rats with aortic coarctation–induced hypertension at 12 days after coarctation. In contrast, the U46619-induced contraction of aortic rings from hypertensive rats at 90–113 days after coarctation was diminished, particularly at submaximal concentrations of the agonist. As expected, U46619 did not contract rings of aorta that were concurrently exposed to SQ29548 (1 μM).

Discussion

This study in rats with aortic coarctation–induced hypertension shows that the maximal contractile response to angiotensin II in rings of descending thoracic aorta is increased in the early phase of the hypertension, at 12 days after coarctation, and decreased in the late phase of the hypertension, at 90–113 days after coarctation. The study also shows that removal of the endothelium by rubbing increases the contractile response to angiotensin II in aortic rings of sham-operated normotensive rats and hypertensive rats at 90–113 days after coarctation but decreases the response to angiotensin II in aortic rings of hypertensive rats at 12 days after coarctation. Thus, it appears that the endothelium attenuates aortic smooth muscle responsiveness to angiotensin II in normotensive rats and rats in the late phase of aortic coarctation–induced hypertension, while amplifying the responsiveness of aortic smooth muscle in the early phase of the hypertension. In agreement with the notion that the endothelium exerts regulatory control of both an inhibitory and a stimulatory nature on vascular responsiveness to angiotensin II, removal of the endothelium was reported to attenuate the constrictor effect of the peptide in canine cerebral arteries and to augment the constrictor effect in isolated preparations of rat aorta and bovine coronary artery.

The vascular endothelium is a known source of vasoactive substances that are putative mediators or modulators of the vascular effects of various vasodilator and vasoconstrictor hormones. Additionally, endothelial cells have been shown to express angiotensin II receptors, which are linked to mechanisms of prostaglandin synthesis and the release of a yet to be identified dilator factor for rat cerebral arteries. The inhibitory influence of the endothelium on vascular responsiveness to angiotensin II has been attributed to the manufacture of an endothelium–derived relaxing factor, presumably nitric oxide, which counteracts angiotensin II–induced contraction of vascular smooth muscle. Similarly, the magnifying influence of the endothelium on vascular responses to angiotensin II may be attributed to the endothelium–dependent generation of factors that contribute to the constrictor effect of angiotensin II.
The list of vascular smooth muscle contracting factors that are implicated in mechanisms of endothelium-dependent vasoconstrictor responses includes endothelin,20 superoxide anion,21 and eicosanoids.22-23 In the present study, we found that both indomethacin and SQ29548 (an inhibitor of cyclooxygenase and a blocker of TXA\(_2\)/prostaglandin endoperoxide receptors, respectively) selectively attenuated the contractile response to angiotensin II in aortic rings of hypertensive rats at 12 days after coarctation. These effects of indomethacin and SQ29548 are not the result of nonspecific inhibition of vascular reactivity since neither agent reduced the contractile response to phenylephrine in aortic rings of sham-operated and hypertensive rats or to angiotensin II in aortic rings of sham-operated rats and hypertensive rats at 90–113 days after coarctation. More likely, attenuation by indomethacin and SQ29548 of the angiotensin II–induced contraction of aortic rings taken from hypertensive rats at 12 days after coarctation is attributable, respectively, to inhibition of the synthesis and blockade of the constrictor actions of vascular prostanoids that activate the TXA\(_2\)/prostaglandin endoperoxide receptor. A corollary of this conclusion is that the augmented constrictor effect of angiotensin II in aortic rings of rats in the early phase of aortic coarctation–induced hypertension is mediated, at least in part, by prostanoids that stimulate TXA\(_2\)/prostaglandin endoperoxide receptors.

It is of interest to note that removal of the endothelium from aortic rings of hypertensive rats at 12 days after coarctation, which by itself reduces angiotensin II–induced contractions, precluded the TXA\(_2\)/prostaglandin endoperoxide receptor blocker SQ29548 from further attenuating the contractile response to angiotensin II. One interpretation of this finding is that in such animals, the endothelium is necessary for expression of the prostanoid-dependent component of the angiotensin II–induced contraction of aortic rings. The conclusion that part of the constrictor effect of angiotensin II in aortic rings of rats in the early phase of aortic coarctation–induced hypertension is related to endothelium-dependent mechanisms of vasoconstriction implemented by prostanoids implies that the vascular synthesis or responsiveness to such prostanoids is increased in this model of hypertension. The results of the present study argue against the latter possibility since direct activation of TXA\(_2\)/prostaglandin endoperoxide receptors with U46619 elicited similar contractile responses in aortic rings of normotensive rats and hypertensive rats at 7–14 days after coarctation.

The identity of the prostanoids mediating endothelium-dependent vasoconstrictor responses is not well established. Inhibitors of thromboxane synthase reduce constrictor responses to angiotensin II and various other agonists in canine cerebral arteries14,24 and to acetylcholine in rabbit intrapulmonary arteries25 suggesting that TXA\(_2\) contributes to the constrictor effect of such agonists. In the present study, angiotensin II was found to stimulate endothelium-dependent release of TxB\(_2\) from aortic rings of sham-operated normotensive rats and rats in the early phase of aortic coarctation–induced hypertension, an effect that was greater in the hypertensive than in the normotensive animals. Yet, the thromboxane synthase inhibitor CGS13080 (10 \(\mu\)M), which reduced to less than 10% of control the release of TxB\(_2\) from angiotensin II-stimulated rings of aorta taken from hypertensive rats at 12 days after coarctation, did not attenuate the constrictor effect of the peptide in any of the experimental groups. Similarly, other investigators have shown that inhibitors of thromboxane synthase do not affect the prostanoid-mediated constrictor response to acetylcholine in the aorta of spontaneously hypertensive rats26,27 suggesting that prostanoids other than TXA\(_2\), presumably a prostaglandin endoperoxide,27,28 mediate the constrictor effect of acetylcholine.

In the present study, contribution of a prostaglandin endoperoxide to the constrictor effect of angiotensin II in aortic rings of rats in the early phase of aortic coarctation–induced hypertension is indirectly supported by the finding that blockade of TXA\(_2\)/prostaglandin endoperoxide receptors with SQ29548 attenuates the constrictor effect of the peptide, whereas inhibition of thromboxane synthase with CGS13080 does not. Yet, a role for TXA\(_2\) in the mechanism of angiotensin II–induced contraction of aortic rings cannot be excluded totally because the functional consequence of diminished TXA\(_2\) synthesis due to inhibition of thromboxane synthase may be obscured by an attendant increase of prostaglandin endoperoxides.

The conclusion that an endothelium-dependent, prostanoid-mediated, mechanism contributes to the constrictor effect of angiotensin II on rings of descending thoracic aorta may or may not apply to resistance arterial vessels of hypertensive rats at 12 days after aortic coarctation. If it does, the blood pressure of rats in the early phase of aortic coarctation–induced hypertension may be expected to fall with the administration of blockers of TXA\(_2\)/prostaglandin endoperoxide receptors due to interference with the expression of the prostanoid-mediated component of the vasoconstrictor action of angiotensin II. Relative to this point, we reported recently that treatment with SQ29548 selectively decreases the blood pressure of rats with aortic coarctation–induced hypertension at 7–14 days after coarctation, an effect that was positively correlated with the prevailing plasma renin activity.29 Thus, the possibility arises that in such a model of angiotensin II–dependent hypertension, an endothelium-dependent, prostanoid-mediated mechanism of vasoconstriction contributes to the increase of blood pressure.

In summary, the present study documents that the maximal contractile response to angiotensin II is increased in the early phase of aortic coarctation–induced hypertension in rats at 12 days after coarctation and decreased in the late phase of the hypertension at 90–113 days after coarctation. The
angiotensin II–induced contraction of aortic rings from hypertensive rats at 12 days after coarctation was selectively diminished in rings without endothelium; it was also selectively decreased either by the cyclooxygenase inhibitor indomethacin or by the blocker of TxA₂/prostaglandin endoperoxide receptors SQ29548 but not by the thromboxane synthase inhibitor CGS13080. The data suggest that the angiotensin II–induced contraction of aortic rings of rats in the early phase of aortic coarctation–induced hypertension relates, at least in part, to activation of an endothelium-dependent mechanism of vasoconstriction, which is implemented by prostanoids that stimulate contraction of vascular smooth muscle via activation of TxA₂/prostaglandin endoperoxide receptors.

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References


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